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ABSTRACTS OF WORLD MEDICINE

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ABSTRACTS OF WORLD MEDICINE

This journal is planned to provide the reader with a selection of abstracts of the more important articles appearing in medical periodicals published in different parts of the world. Comment by the abstracter, when thought necessary, is inserted between square brackets, usually at the end of an abstract. In some instances only the titles of articles are provided.

The titles of journals are given in full and also abbreviated according to the rules adopted in the *World List of Scientific Periodicals* and in *World Medical Periodicals*. The titles of articles from foreign journals are translated into English.

This journal is essentially a guide to work in progress in the world's medical centres. No abstract can be regarded as a substitute for the article abstracted. For complete information the original article must be consulted. Our aim is to give the reader sufficient details in an abstract to enable him to judge whether the original is, for him, worth reading in full.

The abstracts are grouped in broad classifications and, so far as possible, those dealing with medical and surgical aspects of the same problem appear together under the same heading. The specialist will, it is hoped, learn from this journal of work done in other fields as well as in his own. The general practitioner will be able to keep abreast of modern knowledge in the various specialties. The representation in one journal of the several aspects of Medicine will, it is believed, give an integrated picture of the whole, necessary in this age of specialization.

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Pathology

EXPERIMENTAL PATHOLOGY

1230. **Chronic Sodium Chloride Toxicity: Hypertension, Renal and Vascular Lesions**
G. R. MENEELY, R. G. TUCKER, W. J. DARBY, and S. H. AUERBACH. *Annals of Internal Medicine* [*Ann. intern. Med.*] **39**, 991–998, Nov., 1953. 4 figs., 16 refs.

In the experiments here described from the Vanderbilt University School of Medicine, Nashville, Tennessee, the authors sought evidence to support their hypothesis that excessive consumption of sodium chloride may be a factor in the causation of human degenerative diseases. Seven batches, each of 30 male rats, were given diets containing all their nutritional requirements, but with the sodium chloride content varying from 0·01% by weight up to 9·8%. The diet was well taken by all the groups.

The animals on the high-salt diets all had polyuria and polydipsia. After 2 to 3 months massive oedema developed in 18% of the 90 rats on diets containing 7% or more of salt. These animals were anaemic, their blood plasma was grossly lipaemic, and they exhibited hypertension. Many of them were in a state of nitrogen retention, presumably owing to renal failure. The other animals showed a degree of hypertension related to the level of salt intake. Animals taking the three diets highest in salt content showed foam-cell degeneration of the renal glomeruli with, later, degeneration of the tubules. Arterioles developed changes similar to those seen in malignant hypertension in man and showed widespread arteriolosclerosis. Further studies are in progress. *C. L. Cope*

1231. **Influence of Protein Metabolism on Bacterial Allergy. Its Relation to Cortisone Desensitisation**
D. A. LONG. *Lancet* [*Lancet*] **1**, 231–234, Jan. 30, 1954. 4 figs., 18 refs.

It has been shown that ascorbic acid depresses the sensitivity to tuberculin (as measured by the size of the skin reaction) of guinea-pigs injected with B.C.G., and that this desensitizing action is antagonized by a factor present in cabbage which apparently prevents the oxidation of ascorbic acid to dehydroascorbic acid; this factor is in turn antagonized by cortisone, which thus permits the decrease in sensitivity brought about by ascorbic acid to take place. Further experiments carried out at the National Institute for Medical Research, London, have shown that skimmed milk has properties similar to those of cabbage, as also has methionine, which is present in both. On the other hand ethionine, an antimetabolite to methionine, antagonizes the action of cabbage and skimmed milk in the same way as cortisone. The "cabbage factor" and the similar factor present in skimmed milk are therefore thought to be probably identical with methionine.

By analogy with the action of alloxan in diabetes, the author presents the hypothesis that cortisone depresses sensitivity to tuberculin in the guinea-pig by interfering with the anabolism of glutathione. The resulting fall in glutathione concentration in the tissues would increase the oxidation of ascorbic acid to dehydroascorbic acid, which inactivates phosphoglucomutase, resulting in an increase in the tissue concentration of glucose-1-phosphate, which has a desensitizing influence.

H. Herxheimer

CHEMICAL PATHOLOGY

1232. **Clinical Evaluation of the Blood Cell Carboxypeptidase Inhibitor Test for Malignant Neoplasia**
J. C. BALLIN, R. N. FEINSTEIN, and N. E. WARNER. *Cancer Research* [*Cancer Res.*] **13**, 784–788, Nov., 1953. 1 fig., 10 refs.

The results of blood cell carboxypeptidase inhibitor (CPI) assays of the blood of 341 patients are reported. In normal persons and in cases of nonmalignant disease, the titer tends to be high, while in cases of malignant disease, the titer is greatly decreased. False positive results are observed chiefly in cirrhosis, pulmonary tuberculosis, and diabetes. False negative results are seen in 36% of the malignant cases, chiefly carcinomas of the rectum and lung, malignant melanoma, lymphosarcoma, leukemia, and metastatic carcinoma of unknown primary site. All diseases tend to lower the CPI titer. The significance of this observation is discussed. The CPI test is not considered specific enough to be diagnostic for cancer.—[Authors' summary.]

1233. **Estimation of Plasma-insulin by the Rat Diaphragm Method**
J. VALLANCE-OWEN and B. HURLOCK. *Lancet* [*Lancet*] **1**, 68–70, Jan. 9, 1954. 3 figs., 13 refs.

A method for determining the amount of insulin in the blood is described in this paper from the Postgraduate Medical School of London, the basis being the ability of small amounts of insulin to accelerate the utilization of glucose by the isolated rat diaphragm.

The diaphragm was removed from the animal and the thick posterior half discarded. The hemidiaphragm was placed in standard insulin–glucose solution, which was then " gassed " for 5 minutes with 95% oxygen and 5% carbon dioxide. After a further period of 90 minutes at 37° C. the residual glucose in the solution was estimated and the diaphragm was dried and weighed; the glucose uptake over the incubation period was then calculated in relation to dry weight of the diaphragm.

For estimation of insulin in plasma, venous blood was drawn off in a heparinized syringe, the blood sugar estimated, and the plasma separated. Thereafter the plasma was handled in the same way as the standard insulin solution.

A direct relationship was found between the insulin level and the corresponding blood sugar level in the normal fasting subject. There was, however, a wide variation in the plasma insulin value obtained one hour after administration of 50 g. of glucose by mouth. In some cases the insulin value was high and the blood sugar level was still above that in the fasting subject, whereas in others the insulin level was much lower and the blood sugar level was the same as or below the fasting level. It is considered that these two groups correspond to the two types of normal individual response to the glucose tolerance test—the slow and the quick reactions.

R. B. Lucas

1234. **The Viscosity of a Test-meal. Its Influence on Gastric Secretion and Emptying**
J. N. HUNT. *Lancet* [*Lancet*] **1**, 17–18, Jan. 2, 1954. 1 fig., 7 refs.

Some of the mixtures commonly used for test meals contain relatively inert materials which give viscosity to the meal but often introduce technical difficulties into the manipulation and analysis of samples. It would therefore be of considerable advantage if these materials could be omitted without altering the pattern of gastric behaviour.

At Guy's Hospital, London, a series of test meals were given on successive days to 5 healthy volunteers; the whole of the gastric content was recovered after different intervals of time on different days, and the concentration of acid, chloride, and pepsin was determined. (The technique for the serial test meal was that of Hunt and Spurrell, *J. Physiol.*, 1951, **113**, 157.) From the amounts of acid, chloride, and pepsin present, together with those estimated to have passed into the duodenum during the preceding interval, the amounts secreted were assessed and from these findings a serial record of gastric activity was obtained.

Three types of test meal were used: (1) the standard meal (sucrose and the dye phenol red) with pectin to give a viscosity of 40 centistokes at 37° C.; (2) the standard meal without pectin; and (3) the standard meal with gum tragacanth to give the same viscosity at 37° C. as that of the meal containing pectin.

In each subject the emptying pattern of the stomach, the pattern of secretion of the parietal component, pepsin, and the pattern of the non-parietal secretion (the combined products of all the secretory cells of the gastric mucosa except the parietal cells) were virtually indistinguishable for the three types of meal. Since the omission of pectin from a phenol-red meal did not alter the gastric response or pattern of gastric activity, and further since the gastric response to a pectin–phenol-red meal is similar to the response to a gruel meal, the author suggests that much time could be saved in hospitals where the gruel fractional test meal is traditional by substituting a watery phenol-red meal. *A. Ackroyd*

1235. **Excretion of Urinary Pepsinogen (Uropepsin) in Cases of Peptic Ulceration and of Macrocytic Anaemia**
D. H. MACKENZIE. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **34**, 596–598, Dec., 1953. 16 refs.

The excretion of urinary pepsinogen was examined in 76 cases. The assay appears of no value in the diagnosis of peptic ulcerations. The enzyme was absent from the urine of cases of pernicious anaemia. The assay would be a valuable diagnostic aid in certain cases of macrocytic anaemia.—[Author's summary.]

1236. **Urinary Excretion of Acid Phosphatase**
O. DANIEL, P. R. N. KIND, and E. J. KING. *British Medical Journal* [*Brit. med. J.*] **1**, 19–21, Jan. 2, 1954. 5 refs.

In an investigation carried out at the Postgraduate Medical School of London 4 healthy adult males aged 24 to 35 were shown to excrete a considerable amount of prostatic (formol-stable) acid phosphatase in their urine. The results of estimations made on midstream specimens and catheter specimens from the bladder, in both of which the presence of prostatic secretion was considered unlikely, suggested that only one-third to one-fifth of the total acid phosphatase excreted could be attributed to the direct addition of prostatic secretions to the urine in voiding. The daily average excretion of acid phosphatase by these 4 healthy subjects was 1,462 units, whereas 10 patients aged 65 to 85 with benign prostatic hypertrophy excreted a daily average of 262 units and 7 patients aged 56 to 90 with carcinoma of the prostate excreted a daily average of only 128 units despite an increased serum acid-phosphatase level. Deterioration of renal function was accompanied by a further decrease in the excretion of urinary acid phosphatase. It was also found that 9 apparently healthy women aged 23 to 60 excreted a daily average of 217 units of formol-stable acid phosphatase, 8 women with carcinoma of the breast a daily average of 132 units, and 5 women with carcinoma of the breast and bony metastases a daily average of 227 units. The fact that formol-stable acid phosphatase is excreted by women is held to indicate that there must be some source other than the prostate [but no suggestions are put forward as to the nature of this source]. *Ernest T. Ruston*

1237. **Colorimetric Method for Determination of Aureomycin, Carbomycin, Erythromycin, and Terramycin in Aqueous Solution**
D. PERLMAN. *Science* [*Science*] **118**, 628-629, Nov. 20, 1953. 5 refs.

HAEMATOLOGY

1238. **Osteoblasts and Osteoclasts in Bone Marrow Aspiration. Previously Undescribed Cell Findings in Paget's Disease (Osteitis Deformans)**
M. A. RUBINSTEIN, A. SMELIN, and A. L. FREEDMAN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **92**, 684–696, Nov., 1953. 10 figs., 20 refs.

Two new types of cell found in bone marrow aspirated from patients with osteitis deformans are here described. In the investigation of 8 cases of osteitis deformans at the Montefiore Hospital, New York, histological examination of a smear of bone marrow aspirated from the iliac bone involved revealed large mononuclear cells and giant multinucleated syncytial forms.

The individual mononuclear cell is ovoid, measures 25 to 50 μ at its greatest diameter, and has hazy cytoplasmic borders. The nucleus is round, with a diameter of 12 to 16 μ, is located eccentrically, and frequently appears to have been partially excluded from the cytoplasm. These cells may occur singly or in clumps of two or three, the total number varying inversely with the haematopoietic activity of the marrow. They are not found in bones in which there is no radiological evidence of Paget's disease.

The syncytial cell forms may be over 200 μ in diameter and contain as many as 100 nuclei, which are of uniform size and are distributed haphazardly throughout the syncytium. These cells were found in 3 of the 8 cases. It is presumed that the mononuclear cells correspond to osteoblasts and the multinucleate forms to osteoclasts.

The authors suggest that the finding of these cells may be of help in the diagnosis of Paget's disease.

[The article is well illustrated.] *E. G. Rees*

1239. **Studies on Platelets. XI. Antigenicity of Platelets and Evidence of Platelet Groups and Types in Man**
M. STEFANINI, G. I. PLITMAN, W. DAMESHEK, J. B. CHATTERJEA, and I. B. MEDNICOFF. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **42**, 723–738, Nov., 1953. 6 figs., 21 refs.

That the blood platelets are antigenic is suggested by the results of experiments which have shown the development of (1) specific agglutinins against heterologous platelets in animals, and (2) of iso-agglutinins and auto-agglutinins in patients who have received mutiple platelet transfusions. The demonstration of this antigenicity suggests that there are probably different groups and types of platelets.

In the work here described, which was carried out at Tufts College Medical School, Boston, evidence is presented to show the existence of two naturally occurring platelet agglutinins in human plasma which give four platelet groups comparable with, but unrelated to, the ABO groups of the erythrocytes. By the use of immune platelet agglutinins obtained from patients who had received multiple platelet transfusions, 6 serological types of platelet were distinguished. However, the platelet–agglutinin reaction needs further elucidation, since the authors showed *in vivo* that patients with platelet agglutinins quickly disposed of transfused type-compatible platelets, yet plasma from these patients injected into type-compatible normal recipients caused thrombocytopenia. In some cases of idiopathic thrombocytopenic purpura a platelet auto-agglutinin was detected. In 5 out of 9 such cases the auto-agglutinin disappeared after the performance of splenectomy.

The authors emphasize that these findings are of a preliminary nature and "must be interpreted with extreme caution and criticism". *I. Dunsford*

MORBID ANATOMY AND CYTOLOGY

1240. **Neuroepithelioma. Its Place in the Histogenetic Classification of Primary Neuroectodermal Brain Tumors**
J. H. GLOBUS and R. M. CARES. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath.*] **12**, 311–348, Oct., 1953. 27 figs., 47 refs.

In criticism of a classification of cerebral tumours recently proposed by Kernohar and Sayre and as an introduction to the detailed presentation of 6 cases of that rare form of cerebral tumour, the neuroepithelioma, the authors describe at some length the histogenesis and cytology of the neural tube and the tumours derived from it. The rarity of neuroepithelioma may be judged from the fact that in 642 primary cerebral neoplasms seen by the authors at the Mount Sinai Hospital, New York, they were able to identify only 6 examples of this tumour, while Cushing found only 2 examples among 673 cerebral gliomata.

The 6 examples here described occurred in patients ranging in age from 2½ months to 59 years and were located in various parts of the brain, in one case involving the spinal cord. The duration of symptoms from onset to death was very short, the minimum being 6 weeks and the maximum 9 months. Macroscopically, the tumours were infiltrative, their margins being ill-defined. Microscopically, the cell components fell into 9 cell types, all the tumours being pleomorphic. The predominant cell was a primitive one, of the epithelioid, "parent-cell" type. All the tumours contained this cell, as well as germinal cells displaying mitotic activity and spongioblasts. In most of the tumours varying numbers of "naked-nucleus" cells, large and small neuroblasts, ependymal spongioblasts, and giant cells were seen. Well-formed glial fibre network occurred in 3 tumours. "Rosettes" were present in 2 instances, while one of the tumours contained a pigmented epithelium of the choroidal type.

The pleomorphism of these tumours was analogous to the normal development of nerve-tissue cells, in that the tumour cells, because of their dual activity of multiplication and differentiation, simulated the development of nervous tissue along neuronal and spongioblastic (glial-derivative) lines. The authors maintain that the histogenesis of these tumours offers a comparison with normal histogenesis and thus affords a means of classifying primary cerebral neoplasms.

[Their arguments should be read in the original paper.] *Ruby O. Stern*

1241. **The Histopathological Development of the Fibro-hyaline Masses of Pseudotumoral Silicosis.** (Sur le développement histopathologique des masses fibro-hyalines de la silicose pseudotumorale)
A. POLICARD and A. COLLET. *Presse médicale* [*Presse méd.*] **61**, 1503–1505, Nov. 18, 1953. 6 figs.

At the Centres de Recherches des Charbonnages, Paris and Verneuil, a histological study was made of 42 cases of massive silicosis in which there was no " classic " evidence of tuberculosis (caseation, tubercles, or giant cells). From this study the authors reached the conclusion that in the development of massive fibrosis two kinds of dust deposit are concerned, those poor in silica and those rich in this substance. In the deposits associated with dusts relatively poor in silica, the dust is simply enveloped by reticulin fibres, which later develop into collagen. In the case of the reaction to silica-rich deposits the process starts in much the same way, but degeneration soon occurs in the deposit; the dust particles no longer remain in little groups representing the original macrophages, but disseminate, and the degenerated area becomes acellular, although there may be intermediate dust deposits surrounding it. The two contrasting types of reaction can usually be distinguished, although there are intermediate varieties.

Around the degenerated deposit there is a peripheral inflammatory reaction in which the process of fibrosis continues and may invade the deposit itself. In many cases this represents a normal scarring process following inflammation, but in other cases this scarring is accompanied by a process in which there is an exuberant production of fibro-hyaline tissue, sometimes preceded by normal collagenous fibres. This fibrosis is entirely devoid of mineral dust and appears to develop apart from the direct action of the dust; it is this fibro-hyaline tissue which constitutes the main bulk of massive fibrosis. There is thus a distinction between the fibrosis in the dust deposit, which develops by the metaplasia of reticulin, and the fibro-hyaline tissue of massive fibrosis, which is a form of neoplasia.

This concept of the development of massive fibrosis, although unexplained in terms of biological mechanism, explains the development of massive fibrosis in certain cases before silicotic nodules have developed. As the authors remark, why this massive fibrosis should develop in some subjects and not in others remains a mystery.

C. M. Fletcher

1242. **Fibro-anthracosis of the Lungs in Elderly Individuals in a Smoky City**
T. J. MORAN. *Diseases of the Chest* [*Dis. Chest*] **24**, 558–563, Nov., 1953. 4 refs.

Study of a series of 770 consecutive autopsies on elderly individuals with an average age of 60 years from the City of Pittsburgh shows an autopsy incidence of some degree of fibroanthracosis in 97 subjects or 12·6%. In 6 instances fibroanthracosis was the sole cause of death and in 2 other instances the principal cause of death, a fatal incidence of 1·0%. In 2 additional instances fibroanthracosis was listed as a contributory cause of death. Analysis of the causes of death in the 97 subjects with fibroanthracosis indicates that the presence of fibroanthracosis in the lungs does not increase the incidence of or predispose to death from other lung diseases such as pneumonia, tuberculosis, and bronchogenic carcinoma.

Fibroanthracosis was found in only 7 females, and in each of the 7 women lung damage was slight and had no effect on the patient's death. Most of the fatal cases of fibroanthracosis occurred in coalminers. The mechanism of death was congestive heart failure. Right ventricular hypertrophy was marked in almost all of the fatal examples.

Study of this group of 770 residents of the City of Pittsburgh with an average age at autopsy of 60 years suggests that long-continued exposure to a smoky atmosphere, while it may cause minimal scarring after many years, does not result in any appreciable degree of lung fibrosis. Fibroanthracosis of the lungs, in the Pittsburgh district at least, is an occupational disease, predominantly if not entirely, associated with coal-mining.—[Author's summary.]

1243. **Further Observations on Postoperative Gastritis: Histopathologic Aspects, with a Note on Jejunitis**
E. D. PALMER. *Gastroenterology* [*Gastroenterology*] **25**, 405–415, Nov., 1953. 4 figs., 10 refs.

The histopathological changes in the gastric mucosa after varying types of abdominal operation were studied in 45 patients at the Walter Reed Army Hospital, Washington, D.C. The criterion for selection of the patients was histological evidence of a normal gastric mucosa before operation (2 weeks before in 38 of the cases). Mucosal specimens were obtained with the vacuum-tube biopsy instrument (Palmer, *Amer. J. med. Sci.*, 1950, **219**, 648) the patient being in the fasting state.

Evidence of gastritis was found in the specimens from 22 of the 45 patients, independent of the nature of the lesion or the type of operation performed. The histological picture was characteristic, and indicated that the change started at the junction between foveola and gland. The author states that this gastritis is a static process which is unchanged several years after operation.

L. Michaelis

1244. **Sarcomatous Change in Gastric Ulcers.** (La transformation sarcomateuse de l'ulcère gastrique)
L. FRUHLING and R. MOUTIER. *Archives des maladies de l'appareil digestif et des maladies de la nutrition* [*Arch. Mal. Appar. dig.*] **42**, 1076–1091, Sept.–Oct., 1953. 10 figs., 10 refs.

In a search of the literature the authors have found only 4 or possibly 5 previously reported cases of gastric ulcer undergoing change to sarcoma, which in all cases took the form of lymphosarcoma. Among surgical material studied at the Institute of Pathological Anatomy, Strasbourg, consisting of 1,224 gastric ulcers, 125 ulcers with carcinoma, and 36 gastric sarcomata (32 of the latter being lymphosarcomata) there were 3 cases of gastric ulcer of chronic peptic type in close anatomical relation with lymphosarcoma. The patients comprised a man

of 46 with a history of ulcer of 11 years' duration, a man of 38 with a one-year history of ulcer (including a perforation), and a woman of 43 with a 4 months' history. All are still alive, one after 4 years. In the 2 men radiological evidence of peptic ulcer and of the later development of tumour was obtained. In all the cases the pathological picture was of a large ulcer, macroscopically and microscopically of the chronic peptic type, with histological evidence of a narrow rim of lymphosarcomatous tissue surrounding it.

[In none of these patients has the lymphosarcoma recurred, and it is difficult to escape the suspicion that these cases represent either exaggerations of the lymphoid infiltration which is fairly common around peptic ulcers or examples of the much rarer non-neoplastic, or at any rate benign, granulomatous reaction sometimes seen. The photomicrographs accompanying the paper are unfortunately too poorly reproduced for adequate appraisal.] *Bernard Lennox*

1245. **Icterus of the Brain in the Newborn**
A. E. CLAIREAUX, P. G. COLE, and G. H. LATHE. *Lancet* [*Lancet*] **2**, 1226–1230, Dec. 12, 1953. 4 figs., 18 refs.

The incidence of jaundice of the brain in newborn infants was studied at Queen Charlotte's Maternity and Hammersmith Hospitals, London. Of 376 live-born infants on whom necropsy was performed in the 5-year period 1948–52, 33 had jaundice of the brain, and 24 of these showed evidence of Rh iso-immunization. Pregnancy in the mothers of the infants with haemolytic disease was terminated spontaneously or electively. The remaining 9 infants without haemolytic disease were premature, with birth weights well under 2,500 g.; this group included 3 twins whose partners were jaundiced but survived. The infants with haemolytic disease seldom lived more than 4 days, while the premature infants all died on or after the fifth day of life. Clinical features in the mother and infant are described in detail.

At necropsy the pigment was seen to be distributed throughout the brain as well as in the nuclei in 6 infants with haemolytic disease and in 2 of the premature group. In 2 infants the periventricular white matter of the cerebrum was stained and in one the peri-aqueductal tissue was yellow; in the remainder various nuclear structures were involved. The pigment causing the colouring of the brain was extracted in 2 cases of haemolytic disease and in 2 cases from the premature group. Two pigments were separated by chromatography and examined.

It was found that the predominant (slow-moving) pigment in jaundiced brains behaved identically with bilirubin and reacted indirectly to Van den Bergh's test. The absorption curve of this brain pigment in the visible range was the same as that of bilirubin, but in the ultraviolet range it exceeded that of bilirubin, this difference being attributed to materials eluted with the pigment from the chromatographic column. The second pigment reacted directly to Van den Bergh's test, but was present in smaller quantities than the first. Examination by the same technique of the pigment from the serum of 9 cases of erythroblastosis foetalis showed that bilirubin predominated in 8 cases, but the second (fast-moving) pigment varied markedly in amount, and in one case exceeded the bilirubin in quantity. It was found that some substance in the brain, probably a lipid, had an affinity for bilirubin but not for direct-reacting bile pigment obtained from the serum of a patient with obstructive jaundice. No difference in concentration of the bilirubin-retaining material could be detected in various parts of the brain. Large amounts of brain lecithin, cephalin, cerebroside, cholesterol, and neutral fat showed no affinity for bilirubin.

Walter H. H. Merivale

1246. **The Histologic Lesion of Cholemic Nephrosis**
T. W. HOLMES. *Journal of Urology* [*J. Urol.* (*Baltimore*)] **70**, 677–685, Nov., 1953. 4 figs., 4 refs.

The renal changes in obstructive jaundice were studied at Alexander Blain Hospital, Detroit. Of 26 rats in which the common bile duct was ligated, 21 developed jaundice. The jaundice was not invariably fatal; in 3 animals it cleared entirely. All the animals were killed and the kidneys examined at necropsy.

The renal lesions included, in addition to cloudy swelling of the tubular epithelium and pigmented tubular casts, definite hyperplasia and hypertrophy of the epithelium lining the Bowman's capsules, which was most marked in rats that had been jaundiced for more than a week. Minimal glomerular changes were observed in the 5 rats which did not develop jaundice. In only 3 of the animals were there no glomerular capsular lesions. In 2 of these the jaundice had cleared entirely; the third died rapidly, after having been jaundiced for 2 days. The changes are thus, up to a point, reversible.

W. Skyrme Rees

1247. **Histochemical Studies of Human Skin. II. The Intercellular Space.** (Études histochimiques de la peau humaine. II. Les espaces intercellulaires)
A. DUPRÉ. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph.* (*Paris*)] **80**, 490–500, Sept.–Oct., 1953. 10 figs., 29 refs.

Continuing his histochemical investigations into the structure of healthy human skin (see *Ann. Derm. Syph.* (*Paris*), 1953, **80**, 263; *Abstracts of World Medicine*, 1954, **15**, 4) the author studied sections of skin from the palms and soles stained by the MacManus method and with Sudan black B and a variety of other lipid stains. He also examined sections for birefringence, with Baker's acid-haematin test, and for autofluorescence in ultraviolet light. He reports that the space between the epidermal cells is filled with a complex substance consisting of lipids, glucides, and protein. The polysaccharide present, which is not hydrolysed by testicular or microbic hyaluronidase, is Type-B chondroitin sulphuric acid, not hyaluronic acid. This intercellular " cementing substance " is indispensable to the life and cohesion of the epidermal cells: from alterations in its structure many dermatoses (especially bullous) probably originate. It condenses on the " filaments of union " to form the nodules of Bizzozero or desmosomes.

James Marshall

Bacteriology

1248. **Virulence of Tubercle Bacilli Recovered from Patients Treated with Isoniazid**
W. STEENKEN and E. WOLINSKY. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **68**, 548–556, Oct., 1953. 14 refs.

During experiments carried out at the Trudeau Foundation Laboratories, New York, the authors observed that although the growth characteristics and colonial morphology of the H37Rv strain of *Mycobacterium tuberculosis* were unchanged when the organisms were made highly resistant to isoniazid by 10 serial transfers, becoming capable of growth in a concentration of 50 μg. of the drug per ml., yet they were avirulent on injection into guinea-pigs. This avirulence was maintained in subsequent transfers of the strain in a drug-free medium. A further study of the virulence of strains of tubercle bacilli isolated from the sputum of patients before and during isoniazid therapy was therefore undertaken. Experimentally, guinea-pigs in groups of 2 to 5 were infected subcutaneously either with a suspension of tubercle bacilli picked directly from the primary isolation on solid egg-yolk–potato–glycerin medium or with digested and concentrated sputum. The virulence of the infection was judged by the number of animals which died, or by the extent of the disease in survivors killed after 100 days, and was graded as "good", "fair", "slight", or "none". The estimation of the susceptibility of the organisms to isoniazid was by titration in solid media containing graded concentrations of the drug and was defined as "susceptible" (to a concentration of 0·2 μg. per ml.), "slightly resistant" (0·2 to 1·0 μg. per ml.), "moderately resistant" (1·0 μg. per ml.), or "highly resistant" (up to 10 μg. per ml.).

The results showed that there was little difference between the inocula from culture isolates and sputum concentrates. All the strains from 8 tuberculous patients who had never been treated with isoniazid were susceptible to the drug *in vitro*. Of 4 strains showing "good" virulence, 3 were from patients who had had no drug treatment at all and one was from a patient who had been treated for 6 weeks with streptomycin; 3 strains were "fairly" virulent, of which 2 were from patients after 11 to 15 months' treatment with streptomycin and PAS and one from a patient who had had no therapy; and lastly one strain which was "slightly virulent" was from a patient who had received long-term multiple drug therapy and in whom the organisms were highly resistant to both streptomycin and PAS.

Of the 25 strains obtained from patients during treatment with isoniazid, 14 (from 21 patients) showed "no virulence" for guinea-pigs and 9 (from 7 patients) showed "good" virulence. There was no clear correlation between the degree of virulence and resistance to isoniazid *in vitro*, but 6 out of 9 virulent strains were "moderately" or "highly" resistant. There was a direct correlation between the duration of isoniazid therapy and the percentage of patients whose organisms showed resistance to isoniazid *in vitro*, and also with the degree of this resistance. No correlation was apparent between the degree of virulence and the duration of isoniazid therapy.

Some strains were isolated from the same patient both before, and at different times during, treatment with isoniazid. Pre-treatment strains (from only 3 patients) were also examined, of which one showed a progressive loss of virulence, one showed slightly increased virulence, and in another the virulence remained unchanged. All but 5 of the guinea-pigs used gave strongly positive reactions to the intracutaneous injection of 5% old tuberculin. At necropsy of these animals cultures were made from local caseous abscesses or lesions in lymph nodes. Virtually all the strains, although failing to produce progressive disease, could sensitize to old tuberculin and were recoverable 100 days later from local lesions. All the recovered strains were as sensitive to isoniazid as the original cultures.

The authors conclude that exposure to isoniazid is the cause of loss of virulence of the H37Rv strain of *M. tuberculosis* for guinea-pigs, but that it is not correlated with duration of therapy or degree of resistance *in vitro*.

Malcolm Woodbine

1249. **Blocking and Modified Coombs Tests in the Serological Diagnosis of Brucellosis in Man.** (Blockingtest und modifizierter Coombstest in der Serodiagnostik der menschlichen Brucellosen)
F. BÜRKI and H. FEY. *Schweizerische Zeitschrift für allgemeine Pathologie und Bakteriologie* [*Schweiz. Z. allg. Path. Bakt.*] **16**, 945–954, 1953. 19 refs.

Not infrequently the Widal reaction for the presence of antigens to *Brucella abortus* and *Br. melitensis* is negative in spite of well-founded clinical suspicion, or even after it has recently been positive. Two simple and reliable alternative serological methods—a test for blocking of the agglutination reaction as described for *Haemophilus influenzae* by Coca and Kelly (*J. Immunol.*, 1921, **6**, 87) and a modification of the antiglobulin test of Coombs (*Brit. J. exp. Path.*, 1945, **26**, 255)—have therefore been developed by the authors at the State Serum Institute, Berne, and at the Institute of Veterinary Bacteriology of the University of Zürich. Both tests are carried out with the antigen–serum dilutions used in the Widal reaction, which is carried out first, Kahn-test tubes being used for all three. As blocking antigens can be demonstrated best in low serum dilutions it is advisable to start the Widal reaction with a dilution of 1 in 4 or 1 in 5 (after adding the bacterial suspension) in the first tube, and diluting two-fold up to about 1 in 2,560, each tube containing 0·5 ml. of serum dilution and 0·5 ml. of antigen. All sera showing a prozone or giving a negative result in the Widal test are subjected to the blocking and Coombs tests.

For the blocking test 0·1 ml. of a known positive *Brucella* antiserum (human or rabbit) is added to each tube, including the control tube. The best results are obtained if the positive antiserum is added in a dilution known to give less than maximum and more than minimum agglutination. The tubes are incubated at 37° C. overnight and read after a further hour at room temperature. The presence of blocking antibodies in the serum under examination is shown by the absence of agglutination in the lower dilutions, while agglutination of increasing intensity occurs in dilutions of 1 in 20 or 1 in 60 and upwards.

In the Coombs test the *Brucella* antibody, which is contained in the globulin fraction of the patient's serum and is fixed as a globulin complex to the bacilli of the Widal antigen, is demonstrated by precipitating the globulin-fraction–antibody–bacilli complex with an anti-human-globulin serum prepared in rabbits. The negative and control tubes of the Widal test are centrifuged for 20 minutes at 4,000 r.p.m. and the sediment washed 3 times with saline and resuspended in each tube in 1 ml. saline. To each tube is then added 0·1 ml. of a 1-in-100 dilution of anti-human-globulin serum (normal serum may give positive results with lower dilutions of anti-globulin serum). The tubes are incubated at 37° C. overnight and read without shaking. A positive reaction shows as a loose pellicle covering the whole bottom of the tube, whereas a small "button-like" sediment is found if the reaction is negative.

In all, 219 human sera have been examined by the authors in this way. Of these, 20 (9·1%) gave positive Widal reactions for *Brucella* at titres of 1 in 80 or more without a prozone, and 18 (8·2%) with a prozone. A positive reaction to the Coombs test was obtained in 19 Widal-negative sera, 18 of which also gave a positive reaction to the blocking test. The authors strongly recommend these additional techniques in the serological diagnosis of *Brucella* infections. *K. S. Zinnemann*

1250. **Dextran, an Antigen in Man**

P. H. MAURER. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **83**, 879–884, Aug.–Sept., 1953. 22 refs.

Working at the University of Pittsburgh School of Medicine, the author has confirmed the work of Kabat and Berg, who showed (*J. Immunol.*, 1953, **70**, 514) that both native and clinical dextrans are antigenic in man. In the present study, carried out on 55 healthy medical student volunteers, it was found that 3 weeks after the injection of 1 mg. of dextran, 20 out of the 55 subjects showed increased cutaneous sensitivity to the dextran injected, and 18 showed a significant increase (more than 2 μg. per ml.) in the nitrogen precipitable from 1 ml. serum by dextran. No individual developed either sensitivity or significant increase in precipitable serum nitrogen after injection with one of the four clinical dextrans used, known as "R 229".

In general, the greater the increase in precipitable serum nitrogen, the greater the sensitivity. The serum antibodies to dextran were shown to be unchanged after absorption of the serum with pneumococcal polysaccharides, and are therefore not anti-pneumococcal antibodies cross-reacting with dextrans. Anti-dextran antibody persists for long periods in the serum, notwithstanding the fact that dextran is readily metabolized; it is suggested that this may be due to constant stimulation by small amounts of dextran produced by organisms in the intestine. *C. L. Oakley*

1251. **Development of Antibodies in Children Convalescent from Whooping Cough**

J. L. WINTER. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **83**, 866–870, Aug.–Sept., 1953. 1 fig., 11 refs.

Of 50 children whose serum was examined at the Willard Parker Hospital (New York University College of Medicine), New York, during convalescence from whooping-cough, that of only 31 showed an increase in the titre of antibacterial agglutinins against *Haemophilus pertussis*, while an increase in titre of *H. pertussis* antihaemagglutinins was found in the serum of only 7; on the other hand the serum of all of 20 children tested showed an increase (from 2- to 10-fold) in titre of the antibody protecting mice against the effects of intranasal injection of *H. pertussis*. There was no correlation between the titres of the three antibodies. The regularity with which the mouse-protecting antibody appears and the apparent relation between high titre and recovery suggest that this antibody is of importance in the development of immunity to whooping-cough. *C. L. Oakley*

1252. **Recent Studies on Immunization against Poliomyelitis**

J. E. SALK. *Pediatrics* [*Pediatrics*] **12**, 471–482, Nov., 1953. 3 figs., 2 refs.

In an earlier paper (*J. Amer. med. Ass.*, 1953, **151**, 1081) the author described the preliminary results of experiments which showed that it was possible to induce the formation of measurable amounts of antibody to the three known types of poliomyelitis virus in human subjects by the intramuscular injection of tissue-culture fluids treated with formalin and emulsified with mineral oil as an adjuvant. In the present paper from the University of Pittsburgh he reports the results of further experiments showing that it is also possible to stimulate antibody formation with an aqueous vaccine prepared from culture fluid of higher virus content.

To 474 subjects, mostly children, 3 injections of the aqueous vaccine, or 2 of the aqueous vaccine and one of the vaccine containing mineral oil, were given at intervals of one week. There was appreciable antibody response to all three types of virus 3 to 6 weeks after starting vaccination by both methods. The serum antibody level was lower in those subjects who had not been exposed to infection than in those who, before vaccination, had residual antibody from previous exposure. *R. S. Illingworth*

1253. **An Absolute Method for Assay of Virus Hemagglutinins**

S. LEVINE, T. T. PUCK, and B. P. SAGIK. *Journal of Experimental Medicine* [*J. exp. Med.*] **98**, 521-531, Dec. 1, 1953. 3 figs., 14 refs.

Pharmacology

1254. **The Depression of Respiration by the Opiates and its Antagonism by Nalorphine**

R. I. BODMAN. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **46**, 923–930, Nov., 1953. 11 figs., 11 refs.

Pethidine by intravenous injection in the doses commonly employed causes slowing of the rate of respiration with little change in the minute volume. When thiopentone is given there is a reduction in the minute volume without much change in the respiratory rate. Morphine and papaveretum have the same effect on respiration as pethidine, but the duration of the action of pethidine is shorter than that of the other two drugs.

During anaesthesia in a patient whose respiratory rate had been depressed by pethidine, intravenous injection of nalorphine restored the rate to normal within half a minute. There was no initial stimulation, but an abrupt return to normal rate, accompanied by a similarly abrupt restoration of the minute volume. The amount of nalorphine necessary to reverse the respiratory depression caused by 50 mg. of pethidine was determined by administration of 1-mg. doses of nalorphine every two minutes; four such doses were necessary. If another dose of 50 mg. of pethidine was then given there was no respiratory depression. It was also found that 3 mg. of nalorphine restored to normal a respiratory rate which had been reduced by the intravenous administration of 1/3 gr. (22 mg.) of "omnopon." The irregular and hesitant respiration observed in a patient who did not tolerate an endotracheal tube became regular after a dose of pethidine, becoming irregular again after a subsequent dose of nalorphine.

Three volunteers received 3 mg. of nalorphine intravenously; 2 sweated, shivered, and felt sick and giddy for an hour and did not feel well for 3 hours; the third had a "feeling of heaviness in the head and felt slightly unsteady . . . a sensation of unreality supervened for some time". In view of these unpleasant side-effects it was considered unjustifiable to give nalorphine to outpatients.

Some of the possible clinical uses of the drug are briefly discussed. *Norval Taylor*

1255. **The Pharmacology of Pramoxine Hydrochloride: a New Topical Local Anesthetic**

J. L. SCHMIDT, L. E. BLOCKUS, and R. K. RICHARDS. *Current Researches in Anesthesia and Analgesia* [*Curr. Res. Anesth.*] **32**, 418–425, Nov.–Dec., 1953. 5 refs.

Among a number of alkoxyaryl alkamine ethers studied by the authors, pramoxine hydrochloride (*p*-n-butoxyphenyl *gamma*-morpholinopropyl ether) was found to be less active as a surface anaesthetic than some of its congeners, but was also less toxic and irritant. Its effect on the rabbit's cornea was equal to that of cocaine at the same concentration, but lasted twice as long, while it caused no mydriasis in either the rabbit or the guinea-pig. A 1% solution gave good field and nerve-block analgesia in guinea-pigs, but was more irritating than other local analgesics used clinically for this purpose.

Toxic doses of pramoxine caused stimulation of the central nervous system followed by respiratory depression. By the intravenous route the LD_{50} of pramoxine for mice and rabbits was less than that of "cyclomethycaine", another surface anaesthetic. In subacute toxicity tests on mice all animals survived a daily dose, given subcutaneously, of 470 mg. per kg. body weight for 12 days, while 13 animals out of 15 survived when a dose of 942 mg. per kg. was given. There were no significant changes in the internal organs at the end of the experiment. In dogs the daily subcutaneous injection of 50 mg. of pramoxine per kg. for 10 days had no toxic effect. Daily intraperitoneal injections of 80 mg. of pramoxine per kg. for 2 weeks did not inhibit the growth of rats; doubling this dose for a further 5 days still did not affect growth, but there was evidence of irritation in the peritoneal cavity.

Jellies and solutions containing 1% pramoxine hydrochloride applied to mucous surfaces for 5 successive days produced no sign of irritation in rabbits, nor did application of the drug to the scarified skin delay healing. The respiratory epithelium of rabbits tolerated a 3% solution of pramoxine, but a 5% solution caused bronchitis and bronchiolitis in some cases. There was no evidence of sensitization to the drug in guinea-pigs, and it was shown to have a low sensitizing potential in man. Pramoxine is metabolized in the body, less than 5% of the unchanged compound being excreted in the rabbit's urine after the intravenous injection of 25 mg. per kg. Given intravenously, the drug causes a transient fall in the blood pressure, but it is less toxic than other agents, such as tetracaine, to the isolated rabbit auricle.

P. A. Nasmyth

1256. **Counter-irritants. A Method of Assessing Their Effect**

J. G. MACARTHUR and S. ALSTEAD. *Lancet* [*Lancet*] **2**, 1060–1062, Nov. 21, 1953. 14 figs., 7 refs.

In experiments carried out at the University of Glasgow a standard and reproducible pain lasting about 3 minutes was produced by the intramuscular injection of 1·2 ml. of 2·75% saline solution into one forearm, the severity of the pain, assessed on an arbitrary scale, being recorded at 15-second intervals. Various irritants and rubefacients were then applied to the skin of the opposite arm and, when their effect was judged to be maximal, a similar injection of saline was given and the severity of the pain again recorded. Application of radiant heat or galvanic current sufficient to cause cutaneous pain which was "just tolerable" abolished the deep pain of the injection, and the same result was obtained after the

application of 3% oil of mustard to the skin, causing intense irritation. On the other hand application of 5% " trafuril " (thurfyl nicotinate; tetrahydrofurfuryl-nicotinic acid), though causing intense vasodilatation of the skin and a feeling of warmth, had no effect on the deep pain.

It is concluded that the production of skin pain of a certain intensity is necessary for the relief of deep-seated pain by counter-irritation, the production of vasodilatation being of no importance.

V. J. Woolley

1257. **Studies of the Combined Action of Some Antihistaminic Agents**

P. NARANJO and E. BANDA DE NARANJO. *Annals of Allergy* [*Ann. Allergy*] **11**, 699–716, Nov.–Dec., 1953. 2 figs., 39 refs.

At the Central University of Ecuador the antihistaminic action of 8 antihistamine preparations, amongst them mepyramine, promethazine, antazoline, and " trimetone " (prophenpyridamine), was tested singly and in combinations of 2, 3, or 4 of the substances. The intravenous LD_{50}, the protective activity against the injection of 10 mg. histamine per kg. body weight and against the inhalation of a histamine aerosol, and the degree of inhibition of the action of histamine and acetylcholine on the isolated guinea-pig intestine were determined.

When the mixtures of the antihistaminics were given as a protection against histamine aerosol it was found that the combination of 2 of the substances had approximately the same effect as the sum of the effects of the 2 substances given singly. Mixtures of 3 or 4 substances, however, had a greater effect than expected. This " supra-additive " effect is claimed to be due to potentiation. It was particularly pronounced in a mixture containing 40% of mepyramine, 30% of prophenpyridamine, and 30% of " neohetramine " (thonzylamine). The toxicity of this mixture was not potentiated, nor was its anti-acetylcholine activity. *H. Herxheimer*

1258. **Clinical Appraisal of a New Adrenergic Blocking Agent: Effect of Regitine on Digital Blood Flow in Normal Subjects and Patients with Peripheral Arterial Diseases**

C. W. CLARKE, D. R. HAYS, and T. B. VAN ITALLIE. *Circulation* [*Circulation (N.Y.)*] **8**, 715–722, Nov., 1953. 1 fig., 13 refs.

The effect of " regitine " (2-[(*m*-hydroxy-N-*p*-tolyl-anilino)-methyl]-2-imidazoline) on blood flow and pulse volume was studied at St. Luke's Hospital, New York, in 5 normal subjects and 19 patients with various types of peripheral arterial insufficiency. The patients were divided into those suffering from vasospastic arterial disorders, those suffering from organic peripheral arterial disease, and those who had been subjected to sympathectomy for peripheral vascular disease. In the normal subjects regitine injected in doses of 0·6 mg. per kg. body weight produced a threefold increase in blood flow over resting values; indirect body heating also produced a threefold increase, and administration of 50 mg. of " priscol " (tolazoline) was followed by a fivefold increase. In patients in the vasospastic group regitine in doses of 0·75 mg. per kg. increased the blood flow less than did body heating or priscol, while in those with organic disease its effect was approximately the same as that of body heating, but this in turn was less than the increase following the injection of priscol. Regitine is one of the few adrenergic blocking substances with no cholinergic effect, and in this respect differs from priscol. The effect of priscol on pulse rate and blood pressure is quite unpredictable, whereas regitine generally produces a fall in blood pressure and an increase in pulse rate. Among the 24 subjects of this experiment the following side-effects were noted within 30 minutes of injection of the drug: nasal congestion (14), conjunctival injection (12), tachycardia (10), flushing (8), diaphoresis, pilo-erection and chills (2 each), and nausea (1).

Regitine was administered by mouth to 18 patients in an average dose of 300 mg. daily for an average period of 44 days (range 1 day to 9 months). During the treatment period 6 of the 11 patients with intermittent claudication reported improvement, 7 of the 10 patients with night cramps in the legs reported varying degrees of relief, and 9 of the 16 patients with less specific leg pains experienced improvement. However, only 3 of 13 patients complaining of cold extremities and 1 of 5 with trophic changes reported relief, and only in 1 of 15 with absent peripheral pulses did the dorsalis pedis pulse become palpable. Oscillometric studies performed at intervals during treatment showed improvement in only one case. Toxic reactions occurred in 11 of the 18 patients, the most frequent and troublesome being diarrhoea, which occurred in 10 cases and forced discontinuance of treatment in 5. Five patients complained of nausea or vomiting, 4 of dizziness, and 4 of tachycardia, and 2 developed anorexia. The size of the dose had little to do with the occurrence of side-effects. Of the original 18 patients there were only 6 who benefited from the treatment and suffered no side-effects.

Robert Hodgkinson

1259. **Acute Hemodynamic Effects of Hexamethonium in Normotensive Man**

L. RAKITA and S. M. SANCETTA. *Circulation Research* [*Circulat. Res.*] **1**, 499–501, Nov., 1953. 4 refs.

Hexamethonium bromide was administered intravenously to 12 normotensive individuals in a steady state. Complete data are presented for 10 of these subjects. Changes in cardiac output are variable, and the heart rate is generally increased. Brachial and pulmonary artery pressure, and calculated total peripheral and pulmonary resistances, and left ventricular work undergo an over-all decrease. There is marked individual variation in dose-response. These data indicate that hexamethonium lowers arterial pressure in normotensive man primarily by diminishing total peripheral resistance, rather than by diminishing cardiac output.—[Authors' summary.]

1260. **Clinical Experience with a New Anticoagulant, Dipaxin (2-diphenylacetyl-1, 3-indandione)**

L. R. PASCALE and J. H. OLWIN. *Circulation* [*Circulation (N.Y.)*] **9**, 230-237, Feb., 1954. 6 figs., 12 refs.

Chemotherapy

1261. **The Antitubercular Activity of D-Galacturonic Acid Isonicotinyl Hydrazone**
P. P. T. SAH and S. A. PEOPLES. *Journal of the American Pharmaceutical Association* [*J. Amer. pharm. Ass.*] **42**, 612–613, Oct., 1953. 17 refs.

The authors, writing from the University of California College of Pharmacy, San Francisco, describe the preparation of D-galacturonic acid *iso*nicotinyl hydrazone from D-glucuronic acid and *iso*nicotinic acid hydrazide, and briefly report on its physical properties, its acute toxicity in mice, and its activity *in vitro* and *in vivo* against the H37Rv strain of *Mycobacterium tuberculosis*. In mice weighing 20 to 30 g. given the drug intraperitoneally the LD_{50} was about 1·8 g. per kg. body weight. The compound inhibited the growth of tubercle bacilli *in vitro* at a concentration of 0·0002 mg. per ml., and when given in the diet of infected mice in the proportion of 0·023% the effect was comparable to the results obtained with 3,000 units of streptomycin given subcutaneously per week. This new drug is therefore seen to possess low toxicity and high activity.
Malcolm Woodbine

1262. **Susceptibility to Isoniazid and Pathogenicity of Tubercle Bacilli**
H. BLOCH, D. WIDELOCK, and L. R. PEIZER. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **68**, 734–738, Nov., 1953. 2 refs.

Tubercle bacilli isolated from the sputum of 20 patients who were receiving isoniazid treatment were tested for their drug susceptibility *in vitro* and for their pathogenicity for mice upon intravenous infection. Among 20 bacterial strains studied, there was no correlation between drug susceptibility and pathogenicity for mice, on the one hand, and between these two properties and the severity of the disease in the patient from whom the bacteria were isolated, on the other hand.—[Authors' summary.]

1263. **Desensitization to Streptomycin and P.A.S.**
J. CROFTON. *British Medical Journal* [*Brit. med. J.*] **2**, 1014–1017, Nov. 7, 1953. 3 refs.

The problem of the desensitization of persons who have become hypersensitive to streptomycin through contact with the drug in the course of their work is discussed by the author, who describes two illustrative cases, in both of which desensitization was successfully accomplished. Daily intramuscular injections of streptomycin were given, starting with a dose of 10 μg. and working up to 1 g. daily over a period of 35 days in the first case, while in the second the initial dose of 50 μg. was increased to 1 g. over a period of 23 weeks. In the first case described there has been no recurrence of sensitivity despite continued contact with streptomycin over a further period of 3 years.

The author also describes the case of a patient under treatment for pulmonary tuberculosis who became sensitive to both streptomycin and PAS and who was successfully desensitized to both over a period of 33 days. He emphasizes that the problem presented by such cases is much less formidable than that of hypersensitivity in streptomycin-handlers. *R. H. J. Fanthorpe*

ANTIBIOTICS

1264. **Prolonged Penicillemia following the Intramuscular Injection of Benzethacil in Children**
T. E. ROY, G. CRAIG, J. H. O'HANLEY, and J. D. KEITH. *Canadian Journal of Public Health* [*Canad. J. publ. Hlth*] **44**, 370–373, Oct., 1953. 5 refs.

It has already been reported that penicillin is detectable in the blood for some time after intramuscular injection of N:N′-dibenzethylenediamine dipenicillin ("benzethacil"). The present authors describe the results obtained with a single intramuscular injection of 1,200,000 units of benzethacil in 20 patients at the Hospital for Sick Children, Toronto. The ages of the patients ranged from 5½ to 15 years and their weights from 35 to 140 lb. (16 to 64 kg.). Some of them had rheumatic fever, while others were convalescent after orthopaedic treatment; none was receiving other antibiotic therapy.

Penicillin was detectable in the blood for 21 days after injection in most of the cases and for 28 days in some. The serum concentration was low, not exceeding 0·35 unit per ml. 24 hours after injection. It was determined on 51 occasions during the first 16 days and found to be 0·01 unit per ml. or more on only 21 occasions; on 5 occasions it was below 0·05 unit per ml.

The authors suggest that this low serum concentration of penicillin may be effective against highly susceptible organisms, such as Lancefield Group-A streptococci and gonococci. *A. W. H. Foxell*

1265. **Sudden Death following Injection of Procaine Penicillin**
R. C. BELL. *Lancet* [*Lancet*] **1**, 13-17, Jan. 2, 1954. 20 refs.

1266. **The Effect of Cortisone upon the Therapeutic Efficacy of Antibiotics**
E. JAWETZ and E. R. MERRILL. *Science* [*Science*] **118**, 549–550, Nov. 6, 1953. 6 refs.

Cortisone is known to aggravate various infections in man and animals, probably by depressing the host's defence mechanisms. In the present study, undertaken at the University of California School of Medicine, San Francisco, in order to determine whether this action of cortisone might impair the therapeutic efficacy of anti-

biotics, groups of white mice were infected with *Klebsiella pneumoniae* and subsequently treated by the injection of either streptomycin or aureomycin for 3 days.

In the groups of animals which also received cortisone treatment, starting 24 hours before infection, the cure rates were usually lower than in those not given cortisone. The impairment was most apparent when the dose of antibiotic was barely curative when given alone; for example, 2 mg. of aureomycin reduced the mortality from 100% to 12%, but when 1 mg. of cortisone and 2 mg. of aureomycin were given, the mortality was 72%. If sufficient antibiotic was injected, however, the cure rate was not reduced by the administration of cortisone at the same time. These findings, which were equally true of the bacteriostatic drug, aureomycin, and of the bactericidal drug, streptomycin, are in keeping with the view that the host's defence mechanisms contribute materially to the curative action of antibiotics, and further that these mechanisms are depressed by the action of cortisone. *Derek R. Wood*

1267. **The *in vitro* Sensitivity of *H. influenzae* to Five Different Antibiotics**

K. ZINNEMANN. *British Medical Journal* [*Brit. med. J.*] **2**, 1069–1072, Nov. 14, 1953. 34 refs.

The sensitivity tests described in this article were carried out at the University of Leeds with the object of determining the most effective antibiotic for the treatment of infections due to *Haemophilus influenzae*. Recently isolated strains of *H. influenzae* were inoculated into Levinthal broth, incubated overnight, and 4 drops of a 1-in-1,000 dilution in nutrient broth of this culture were spread over the whole surface of each of three horse-blood chocolate-agar plates. Holes were punched at regular intervals round the edge of the medium and filled with dilutions of the antibiotics to be tested. One plate was used for penicillin, one for streptomycin and aureomycin, and the third for chloramphenicol and " terramycin " (oxytetracycline). The standard dilutions employed were 1, 2, 5, and 10 Oxford units of penicillin per ml., and for the other antibiotics 1, 2, 5, and 10 μg. per ml. To enable comparison to be made with other workers' results, the author's results were expressed both as the concentration of antibiotic resulting in " partial inhibition " and also that giving " complete inhibition ", the former term being defined as " a marked zone of inhibition of growth round the punch-holes ", while the latter indicated complete absence of growth within the whole or part of the inhibition zone. Of the 84 strains of *H. influenzae* examined, 34 were capsulated and 50 non-capsulated. The cerebrospinal fluid of children with meningitis provided 21 of the capsulated strains, all of which belonged to Pittman Type b. The remaining 13 strains of this group and the 50 non-capsulated strains came from representative sources and it was considered that they could be regarded as unselected.

The results of both complete and partial inhibition tests, calculated on a weight-for-weight basis, showed that chloramphenicol was by far the most efficacious, penicillin and oxytetracycline came next and were almost equally active, while streptomycin and aureomycin were the least effective. In comparing his results with those of other workers the author draws particular attention to those of Tunevall (*Acta oto-laryng. (Stockh.)*, 1952, **42**, 298) which showed that aureomycin appeared to be somewhat better than chloramphenicol; he suggests that the divergence may be due to the different techniques employed. Turning to a comparison of penicillin and chloramphenicol, the author points out that blood concentrations of penicillin high enough to inhibit most or all strains of *H. influenzae* are very difficult to achieve and maintain, although high concentrations can be obtained in the cerebrospinal fluid by intrathecal injection. On the other hand, the usual oral doses of chloramphenicol give an effective blood concentration of 5 to 10 μg. per ml. It is concluded, therefore, that chloramphenicol is the most effective of the five antibiotics tested against *H. influenzae*. The possibility of undesirable side-effects of the drug must be taken into consideration in the final assessment of chloramphenicol as a therapeutic agent—especially in children—but it is suggested that the danger of causing aplastic anaemia or related blood dyscrasias should be small if administration of the drug is confined to one short course of a few days' duration. *H. J. Bensted*

1268. **Participation of Erythromycin and Carbomycin in Combined Antibiotic Action *in vitro***

V. R. COLEMAN, J. B. GUNNISON, and E. JAWETZ. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **83**, 668–670, Aug.–Sept., 1953. 12 refs.

On the basis of their bactericidal action in various combinations, antibiotics can be divided into two broad groups: (I) that including penicillin, streptomycin, bacitracin, and neomycin; and (II) that including aureomycin, chloramphenicol, and oxytetracycline (" terramycin "). Those in Group I are often synergic and never antagonistic to each other in combination, whereas those in Group II are neither synergic nor antagonistic to each other, although the effect of combination is sometimes additive. Members of Group I may be indifferent, synergic, or antagonistic to members of Group II. (A synergic combination is defined here as one having a bactericidal effect greater than that of 2 to 5 times greater concentrations of each of its components when used alone.)

Erythromycin and carbomycin (" magnamycin ") are new antibiotics which are active against a similar range of organisms and against which resistant variants, mostly showing cross-resistance, are rapidly produced. Simultaneous exposure of bacteria to erythromycin and penicillin or streptomycin having been found to reduce the frequency of development of such resistant organisms, the occurrence of synergism or antagonism when the erythromycin and carbomycin are combined with other antibiotics has been examined at the University of California School of Medicine, San Francisco. The test organisms included *Klebsiella pneumoniae*, *Streptococcus faecalis*, and strains of *Staphylococcus aureus*. Solutions of the antibiotics in 0·85% saline were used, final dilutions being made with broth. Inocula giving a final concentra-

tion of 10^7 to 10^8 organisms per ml. in a total of 15 ml. were used, and viable counts made at intervals during incubation at 37° C. Erythromycin and carbomycin, when acting alone, behaved similarly, exerting a bactericidal effect during the first 24 hours although some bacteria usually survived and subsequently multiplied. When bacteriostatic or slowly bactericidal doses of erythromycin or carbomycin were combined with a rapidly bactericidal dose of penicillin, the bactericidal effect of penicillin was sometimes reduced on all three organisms. A similar antagonism has previously been demonstrated between these drugs and chloramphenicol, aureomycin, and oxytetracycline. Combinations of bacteriostatic doses of erythromycin or carbomycin with bacteriostatic doses of antibiotics of Group I were often additive in effect, the new drugs resembling in this respect the members of Group II. The effect of erythromycin and carbomycin in combination was only negligibly additive, and the addition of chloramphenicol or oxytetracycline to either resulted in no greater an increase in effect than could be obtained with a proportional increase in the dose of the drug acting alone. Group-II drugs are often interchangeable in combinations, but erythromycin or carbomycin could not always replace oxytetracycline or aureomycin. However, the available evidence suggests that these two drugs should be placed in Group II. As with other Group-II compounds, the behaviour of erythromycin and of carbomycin in combination with members of Group I was found to be unpredictable, but in general both showed some form of summation of action against *Staph. aureus*.

Malcolm Woodbine

1269. **Effect of Erythromycin, Thiocymetin, and Three Other Antibiotics on *Leptospira icterohemorrhagiae* in the Chick Embryo**

R. A. Ormsbee. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **83**, 815–816, Aug.–Sept., 1953. 9 refs.

Although penicillin and streptomycin have been reported to be effective against leptospirosis and aureomycin against the carrier state in animals, none of these drugs has proved particularly effective in the treatment of leptospirosis in man. Experiments were therefore carried out at the U.S. National Microbiological Institute to examine the effect of two new compounds, erythromycin and thiocymetin, on *Leptospira icterohaemorrhagiae* and to compare their potency with that of chloramphenicol, aureomycin, streptomycin, and benzyl penicillin.

Tests were performed on groups of 25 to 30 6-day-old chick embryos, which were infected via the yolk sac with a suspension of *L. icterohaemorrhagiae* in doses sufficient to kill control embryos in an average of 4·7 to 4·8 days. Aqueous solutions of the antibiotics were injected by the same route 24 hours later. All embryos dying within 72 hours of the infection were discarded, death being regarded as due to injection trauma. The surviving embryos were candled daily for 13 days, when the tests were terminated. The results showed the drugs to be effective in the following order: erythromycin> benzyl penicillin>streptomycin>aureomycin>thiocymetin>chloramphenicol. Erythromycin was 8 to 40 times more effective than benzyl penicillin, and the authors conclude that it is a potentially valuable aid in the treatment of leptospirosis. *Malcolm Woodbine*

1270. **Inhibition of Cytopathogenic Effect of Poliomyelitis Viruses in Tissue Culture by Antibiotic M-8450**

R. N. Hull and J. M. Lavelle. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **83**, 787–790, Aug.–Sept., 1953. 4 refs.

Working at the Lilly Research Laboratories, Indianapolis, the authors have studied the inhibitory and chemo-prophylactic action of a new mould filtrate, "M-8450", on examples of the three immunological types of poliomyelitis virus, which were grown on tissue cultures in plasma-clot roller tubes, using testicular tissue from immature cynomolgus or rhesus monkeys. The technique is described in detail. The viruses used were two of Type 1 (Duffy and 787), a cytopathogenic Type 2 (YSK), and one of Type 3 (Leon) [but the precise origin of the antibiotic is not specified; this, probably deliberate, vagueness is to be deplored in a communication to a scientific journal]. Several different procedures were followed for bringing the antibiotic and virus into contact, involving dosage before and after infection.

Results of these preliminary studies showed that the antibiotic caused monkey testicular cells in tissue culture to become refractory to the action of all 3 immunological types of poliomyelitis virus. The best results were obtained when the cells were treated 24 hours before the introduction of the virus; when M-8450 was administered 10 minutes before, or simultaneously with, inoculation, little or no protection was afforded. That the antibiotic exerts its effect on the cells and not the virus was shown by the facts that pre-treatment of the cells was necessary for protection and that pre-treatment of the virus had no protective effect, and also by the observation that viable virus could be demonstrated in undamaged, treated cultures 5 days after inoculation; thus M-8450 has no neutralizing effect on the virus itself. The authors find the explanation of its action an intriguing problem, but suggest that the mechanism is probably one of interrupting or preventing some stage of virus multiplication.

Malcolm Woodbine

1271. **Clinical and Laboratory Studies of Infections due to *Pseudomonas aeruginosa* and *Pseudomonas* species**

C. P. Erwin, B. A. Waisbren, and R. Kruse. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **226**, 525–532, Nov., 1953. 6 refs.

In vitro and clinical studies of the effectiveness of antibiotics against *Pseudomonas aeruginosa* and *Pseudomonas* species were presented in this report. Polymyxin B and oxytetracycline were the most effective antibiotics against infections due to *Ps. aeruginosa*. Antibiotics were not effective against the majority of strains of *Pseudomonas* species, but chloramphenicol and neomycin appeared to be the best agents for use against these bacteria.—[Authors' summary.]

Infectious Diseases

1272. **Therapeutic Doses of Gamma Globulin in the Treatment of Measles Encephalitis and Encephalomyelitis. I. A Clinical Study of Forty-one Cases with Follow-up Studies**

L. Odessky, A. V. Bedo, K. G. Jennings, I. J. Sands, P. Rosenblatt, H. Weisler, and B. Newman. *Journal of Pediatrics* [*J. Pediat.*] **43**, 536–568, Nov., 1953. 3 figs., 34 refs.

To explain the comparatively rare development (in less than 0·3% of cases) of encephalitis or encephalomyelitis as a complication of measles the authors suggest several hypotheses additional to those usually offered, namely, that (1) the debilitated state of the patient allows the virus to penetrate the blood–brain barrier; (2) the production of antibodies does not keep pace with the invading virus; (3) the destruction of antibodies is more rapid than their formation; and (4) in rare cases there may be inability to produce gamma globulin. A review of 590 cases of measles reported in the literature showed that the mortality was about 15% and that in some 40% of those patients who recovered there were sequelae.

At the Kingston Avenue Hospital, Brooklyn, New York, of 41 patients severely ill with measles, 27 were treated with gamma globulin. In a control group (14 patients) who received no gamma globulin in the acute phase, 2 patients died (14%) and sequelae occurred in 6 cases (43%). In the first treated group (12 cases) the patients were given 0·07 to 0·30 ml. of gamma globulin per lb. (0·15 to 0·66 ml. per kg.) body weight; in this group 3 (25%) died and sequelae, all mild or moderate, occurred in 3 others (25%). In the second treated group (15 cases), given 0·43 to 1·1 ml. per lb. (0·95 to 2·4 ml. per kg.) body weight, there were no deaths, severe sequelae in 1 case (7%) and mild sequelae in 5 cases (33%); the other 9 patients made a complete recovery.

[A wealth of clinical detail is given in tables and charts but does not lend itself to abstracting. Appraisal of this clinical material subjectively by the authors and objectively by the interested reader must determine the worth of this paper and its conclusions. The series of cases were treated consecutively in time, so that no true controls were available. The advice of a statistician at the planning stage might have resulted in the emergence of some valuable conclusions from this study.]

John F. Loutit

1273. **Intestinal Protozoa in Mentally Deficient Children**

G. D. Belios and W. Cooper. *British Medical Journal* [*Brit. med. J.*] **2**, 805–807, Oct. 10, 1953. 7 refs.

The faeces from 50 mentally deficient children at Harperbury Hospital, Shenley, Hertfordshire, were examined for the presence of intestinal protozoa. The children, aged 5 to 17 years (mean 10 years), had lived in the hospital for an average of 5 years; none had lived in tropical or subtropical countries. Films were prepared from untreated faeces with saline, Lugol's iodine, and a solution of eosin, and also with eosin and iodine after concentration with zinc sulphate solution. In order to detect the cysts of the smaller protozoa, the concentration of the zinc sulphate solution was increased to 51%, specific gravity 1·28. Each specimen was also cultured, the culture being examined after 24 hours.

The following protozoa were found: *Entamoeba coli* in 29 cases (58%); *E. histolytica* in 16 cases (31%); *Endolimax nana* in 10 cases (20%); *Iodamoeba bütschlii* in 9 cases (18%); *Giardia intestinalis* in 7 cases (14%); *Chilomastix mesnili* in 3 cases (6%); and *Enteromonas hominis* in 10 cases (20%). Twelve children were examined more than once, 3 additional cases of infection with *Entamoeba histolytica* being found, bringing the incidence to 40%. [The percentage of *E. histolytica* infections should be 32, the additional 3 infections raising this figure to 38.]

The value of culture in investigations of this kind is demonstrated by the number of infections detected and by the fact that the 10 cases of infection with *Enteromonas hominis* were discovered only by culture. The results obtained by the concentration technique were better than those obtained by direct examination.

The authors believe that the incidence of cases of *E. histolytica* infection is the highest yet reported in Britain. [They present no evidence to show that the results with their zinc sulphate solution were better than those usually obtained.] *R. A. Neal*

1274. **The Treatment of North American Blastomycosis with 2-Hydroxystilbamidine**

I. Snapper and L. V. McVay. *American Journal of Medicine* [*Amer. J. Med.*] **15**, 603–623, Nov., 1953. 14 figs., bibliography.

After reviewing the therapeutic measures at present available for the treatment of North American blastomycosis, the authors give full clinical details of 4 cases of this disorder treated at the John Gaston Hospital, Memphis, Tennessee, with 2-hydroxystilbamidine diisethionate, a less toxic derivative of stilbamidine. The patients were aged 40, 4, 29, and 84 years respectively; three of them suffered from the systemic form of the disease, while in one case it was of the cutaneous variety. The patients were given total quantities of 19·6, 4·3, 8·1, and 4·5 g. respectively of the drug, in fractional doses, over a prolonged period. Extensive biochemical studies carried out during treatment did not reveal any toxic effects—in particular, no evidence of trigeminal neuropathy; the results of treatment were regarded as very satisfactory. The authors were able to establish that *in vitro* 2-hydroxystilbamidine has a definite inhibitory effect on the mould form of *Blastomyces dermatitidis*, and they suggest that the drug may with advantage be combined with aureomycin in severe cases of systemic infection. *S. Karani*

Tuberculosis

RESPIRATORY TUBERCULOSIS

1275. **The Initial Period of Artificial Pneumothorax. The Effect of *para*-Aminosalicylic Acid and Dihydrostreptomycin on the Frequency of Pleural Effusion and on Pulmonary Function**

D. G. BIRATH. *Diseases of the Chest* [*Dis. Chest*] **24**, 245–258, Sept., 1953. 5 figs., 4 refs.

The effect of administration of PAS and dihydrostreptomycin on the incidence of pleural effusion and on pulmonary function in cases of artificial pneumothorax was investigated at Soderby Hospital, Sweden. Between 1948 and 1951 artificial pneumothorax was induced in 266 patients; of this number 105 did not receive chemotherapy, 82 received PAS, and 79 received PAS and dihydrostreptomycin combined.

The main indication for artificial pneumothorax was fresh infiltration with caseation, usually in the upper lobe but not infrequently in the apical segment of the lower lobe. PAS and dihydrostreptomycin were given for about 6 weeks before induction and continued for an average period afterwards of 106 days in the PAS-treated group and 74 days in the group given streptomycin and PAS.

A free space was found at induction in rather more than half the patients receiving chemotherapy and in less than half of the untreated group. Induction was followed by "spontaneous" effusion in 17 of the untreated group, in 7 of the patients given PAS, and in 4 of those given dihydrostreptomycin and PAS. Adhesion section was followed by effusion in 27, 15, and 13 cases in the three groups respectively. The over-all incidense of persistent effusion fell from 27 to 7%. No patient given chemotherapy developed empyema, but this complication was observed in 3 of the untreated patients. Moderate and severe degrees of functional impairment were found only in the untreated group. *T. M. Pollock*

1276. **Artificial Pneumoperitoneum in the Treatment of Pulmonary Tuberculosis. A Late Follow-up of 101 Patients**

J. R. EDGE. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **47**, 202–208, Oct., 1953. 4 refs.

The late results of artificial pneumoperitoneum in 101 cases of pulmonary tuberculosis are reported, the follow-up period being 4 to 9 years. The complications included air embolism (2 cases, with one death) and peritoneal effusion (9 cases, with one death). Puncture of the bowel occurred in one case and there was mediastinal emphysema in one case, but this was mild in degree.

The patients were divided into three groups according to the immediate response to induction of pneumoperitoneum. In Group 1, consisting of 25 patients with the least severe form of the disease, pneumoperitoneum with phrenic crush was the only treatment given. In Group 2, containing 41 patients with more advanced lesions who received the same initial treatment as patients in Group 1, there was definite radiological evidence of improvement, but the results were not considered satisfactory and further active treatment was advised. In Group 3 there were 35 patients with extensive disease; none benefited from induction of pneumoperitoneum.

The follow-up investigation revealed that 9 patients in Group 1 were readmitted to hospital with active disease, refills having been discontinued after an average period of 2 years. In 8 of these cases the relapse occurred a short time after discontinuing refils. Of the 41 patients in Group 2, 8 relapsed, but since the patients in this group had more severe lesions the results are considered to compare favourably with those in Group 1.

The author concludes that if treatment is confined to induction of pneumoperitoneum, then refills must be continued for considerably longer periods than 2 years. *T. M. Pollock*

1277. **A Comparative Study of Various Methods of Administration of Isoniazid.** (Étude comparative des divers modes d'administration de l'isoniazide)

—. PIERRE-BOURGEOIS, G. VALETTE, —. VIC-DUPONT, —. DUBOIS-VERLIÈRE, A. ROY, R. DELMAS, and J. SAVEL. *Revue de la tuberculose* [*Rev. Tuberc. (Paris)*] **17**, 901–915, 1953. 5 figs.

Working at the Hôpital Cochin, Paris, the authors have compared the results of intravenous administration of isoniazid (alone or in association with PAS) and of its administration in suppositories and by mouth in cases of pulmonary tuberculosis. By intravenous infusion either 0·25 or 0·5 g. was given, with or without 15 g. of PAS, over a total period of 3 months, daily for the first month, every 2 days during the second, and every 3 days during the third. A similar routine was followed in treatment with suppositories, each of which contained 0·25 g. of isoniazid, one or two being given at a time.

With intravenous infusion the blood isoniazid concentration attained the same high level whether or not PAS was also given, while significant concentrations were maintained in some cases for a period of 24 hours after the infusion. The concentrations obtained in the blood after administration of the drug by suppository were essentially the same as those obtained with the same dose given orally, reaching a peak 4 hours after administration and falling to zero within 24 hours. Toxic reactions from intravenous therapy were few, and were certainly no more frequent or severe than with oral therapy. On the other hand no toxic symptoms at all were noted from isoniazid given in the form of suppositories. Resistance of the tubercle bacillus to the drug

developed rapidly with perfusions of isoniazid alone, but the incidence was greatly diminished by the addition of PAS. In all, 75 patients were treated, 15 being given isoniazid intravenously alone, 38 being given isoniazid and PAS intravenously, and 22 being treated with suppositories.

The authors consider that while the results of treatment with isoniazid suppositories are comparable to those obtained with the drug by mouth, intravenous administration, especially with PAS, gives much better results than does either of the other routes.

[The numbers of patients in the three groups were small, and the investigation does not seem to have been really adequately controlled.] *G. M. Little*

1278. **Effects of Isoniazid on Patients with Tuberculosis and Mental Illness**
B. HUNT and J. D. WASSERSUG. *New England Journal of Medicine* [*New Engl. J. Med.*] **249,** 1051-1056, Dec. 24, 1953. 3 figs., 5 refs.

1279. **Isoniazid in Tuberculous Psychotic Patients**
M. A. FERRARA and E. B. PETERSON. *New England Journal of Medicine* [*New Engl. J. Med.*] **249,** 1070-1071, Dec. 24, 1953. 4 refs.

1280. **Isoniazid in Pulmonary Tuberculosis**
MEDICAL RESEARCH COUNCIL OF IRELAND. *Irish Journal of Medical Science* [*Irish J. med. Sci.*] **6,** 421–432, Nov., 1953. 9 refs.

A controlled trial of isoniazid was carried out in 31 cases of pulmonary tuberculosis with positive sputum at two hospitals in Dublin and a sanatorium at Newcastle, County Dublin. It was hoped to observe the patients for 6 months, but only 22 of them were available at the end of this period, one of the remaining 9 patients dying in the 4th month and the others being discharged or subjected to surgical intervention. Initially the drug was to be given for 3 months, but this was later extended to 6 months. The daily dosage was 4 mg. per kg. body weight. At the beginning of treatment 9 (29%) of the patients were in " good " condition, and at the end of 6 months this percentage had risen to 50 (11 out of 22). The number of those in " poor " condition decreased during the same period from 8 (26%) to 2 (9%). Improvement in appetite and weight gain were far more marked in recent cases than in advanced cases. The erythrocyte sedimentation rate fell in nearly all cases, but the fall tended to be slow in those with fresh lesions and a high initial reading. Radiologically, 22 of 28 patients examined (79%) showed improvement at the end of 3 months and 17 out of 22 (77%) at the end of 6 months. Of the 22 chronic cases, 17 showed radiological improvement during the first 3 months; cavities were, however, little affected.

The organisms in the sputum were regarded in all cases as being initially sensitive to the drug. At the end of 3 months 10 out of 31 cases (32%) and at the end of 6 months 9 out of 21 (43%) were sputum-negative. The organism in 12 out of 20 cases with positive initial cultures showed resistance at the end of 3 months, and in 10 out of 12 after 6 months. The more chronic the case, the higher the resistance. But those patients with resistant organisms at the end of 3 months showed little clinical deterioration during the next 3 months. This finding, which does not tally with those of other observers, may be due to decreased virulence of the resistant bacilli. There were no reports of toxic effects from isoniazid.

Paul B. Woolley

1281. **Ulceration of the Bronchial Stump After Resection for Tuberculosis**
L. R. ROLL. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69,** 84-91, Jan., 1954. 18 refs.

1282. **Segmental Resection in Pulmonary Tuberculosis. A Preliminary Report**
Y. M. PAUZNER. *Diseases of the Chest* [*Dis. Chest.*] **25,** 78-93, Jan., 1954. 6 figs., 15 refs.

See also Chemotherapy, Abstracts 1262–3

B.C.G. VACCINATION

1283. **The Occurrence of Pulmonary Lesions in BCG-Vaccinated and Unvaccinated Persons**
S. C. STEIN and J. D. ARONSON. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **68,** 695–712, Nov., 1953. 1 fig., 8 refs.

Between 1936 and 1947, under the auspices of the University of Pennsylvania and the Bureau of Indian Affairs, Washington, D.C., an investigation was carried out among North American Indians to determine the value of B.C.G. vaccination in the control of tuberculosis. The results of an investigation of the specific protection afforded by this vaccine, based on a comparison of the mortality rates in vaccinated and unvaccinated persons have already been reported. In the present paper the morbidity from tuberculosis in the two groups (vaccinated 1,540; unvaccinated 1,450) is compared, serial chest radiographs taken at intervals of one year for 9 to 11 years being used for this purpose.

Lesions of primary pulmonary tuberculosis constituted the most common manifestation of the disease in both groups, but were much more frequently observed in the control group. A high incidence of such lesions in one group of Sioux Indians (roughly 5% of the vaccinated subjects) was attributed to the low antigenic value of the vaccine used. The incidence of minimal and moderately advanced tuberculosis was significantly higher among the controls than among the vaccinated. The number of cases of far-advanced tuberculosis was too small to be statistically significant. Miliary tuberculosis was not observed among the vaccinated subjects.

The attack rate was highest in the first two years following vaccination, after which it declined rapidly, becoming relatively constant throughout the period of observation. Even during the first two years the attack rate in the vaccinated group was less than half that in the control group.

As expected, the incidence of primary pulmonary lesions was highest among the younger subjects in both groups, decreasing rapidly with increasing age; the incidence of the reinfection type of pulmonary tuberculosis rose with increasing age. Pleural effusion occurred most frequently in patients in the age groups 10 to 14 and 15 to 19 years. The incidence of primary, minimal, moderately advanced, and miliary tuberculosis was higher among females than among males; there was no difference between the sexes in the incidence of pleural effusion.

It is considered that the results of this investigation provide further evidence of the protective value of B.C.G. vaccination in areas where the standard of living is poor and morbidity from tuberculosis is high.

T. M. Pollock

1284. **The Correlation of the Tuberculin Reaction with Roentgenographically Demonstrable Pulmonary Lesions in BCG-vaccinated and Control Persons**

J. D. Aronson and C. F. Aronson. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **68**, 713–726, Nov., 1953. 9 refs.

In the population surveyed by Stein and Aronson (see Abstract 1283) as many persons as possible in the two groups, besides being examined radiologically, were tested with 0·00002 mg. of purified protein derivative (P.P.D.) and, if negative 48 hours later, were retested with 0·005 mg. of P.P.D.

Among the control subjects in whom definite or suggestive radiological evidence of tuberculosis had been found, a negative reaction to 0·005 mg. of P.P.D. was converted to a positive reaction to 0·00002 mg. of P.P.D. in from 66·6 to 85·1% of cases, and in most of these cases the high level of hypersensitivity to tuberculin was maintained throughout the study. In a small number of cases hypersensitivity increased, fluctuated, or reverted to a negative or doubtful reaction. In many cases (27%) the presence of calcified pulmonary lesions was associated with a negative Mantoux reaction; these lesions were probably not due to tuberculosis. During the study, 55% of those whose radiographs did not show any abnormal shadows remained tuberculin negative throughout. A definite increase in hypersensitivity in a subject who had received B.C.G. vaccination was interpreted as being due to superimposed infection by virulent tubercle bacilli.

A positive reaction to the smaller dose of P.P.D. was seen in a high proportion of the B.C.G.-vaccinated cases in which the radiographs showed evidence of primary or minimal tuberculosis. Among those vaccinated with B.C.G., 93% reacted to one or the other dose of P.P.D. one year after vaccination, and a higher proportion gave a definite positive reaction to the weaker strength; it is thought that this may have been due to a superimposed tuberculous infection which occurred during the first year following vaccination. In a high percentage of cases in the control group, the appearance of pulmonary lesions of all forms of active tuberculosis was associated with a high level of tuberculin sensitivity, concomitant with the discovery of the lesion or with a positive tuberculin reaction noted one year previously. Pulmonary calcification was, however, associated with a lower proportion of positive tuberculin reactions at these times. With the exception of those with calcified pulmonary lesions, only a small proportion of those with radiologically demonstrable pulmonary lesions were tuberculin negative at the time when the pulmonary lesion appeared and these subsequently became tuberculin positive. The authors consider, however, that the absence of a definite tuberculin reaction in the presence of a lesion thought to be tuberculous strongly suggests that the lesion is not tuberculous.

T. M. Pollock

1285. **The Duration of Immunity after B.C.G. Vaccination.** (Die Dauer der Immunität nach BCG-Vaccination)

H. Enell. *Monatsschrift für Kinderheilkunde* [*Mschr. Kinderheilk.*] **101**, 469–473, Nov., 1953. 6 figs.

Since 1945 voluntary B.C.G. vaccination has been available to all Stockholm school-children and has been carried out—usually at the age of 7 to 9 years—in more than 40,000 cases. Starting in 1950 the author, working in the Stockholm School Medical Service, has re-examined the older children (aged 9 to 15) in 7 schools of different types and in different areas, totalling approximately 4,000. This sample was thought to be representative of the population concerned [although no elaborate precautions were taken to ensure that this was so], and only 2·4% had to be excluded from the analysis owing to prolonged absence, eczema, or other reasons. Of the whole population tested, only 16% were tuberculin negative. Of 3,112 B.C.G.-vaccinated children, 3,002 (97·2%) were tuberculin positive, whereas of 843 unvaccinated children, 328 (38·8%) gave a positive reaction, of whom 178 showed no evidence of tuberculous disease, 126 had primary hilar tuberculosis, and the rest had other forms of tuberculous disease; 148 of the 328 had been tuberculin positive before attending school and 52 on first attending, while 28 gave a positive reaction at the end of the first year at school, conversion taking place subsequently in the remaining 100 cases. Of the vaccinated children, 7 (0·16%) had some evidence of active tuberculous infection compared with 42 (6·5%) of the 643 unvaccinated children who had been tuberculin negative on starting school.

Of 312 children who had been successfully vaccinated at school in 1945–6, 4% had become tuberculin negative by 1950–1. Of another group of 312 children who had been vaccinated in 1940–4, before they started school, the proportion who had become tuberculin negative by 1950–1 was again only 4%, in spite of the longer period of observation, but this can probably be accounted for by more frequent opportunities for superinfection in this group, in which there was a high incidence of positive family history of tuberculosis. It is suggested that B.C.G. may be regarded as giving good protection for 7 to 8 years in at least 90% of successfully vaccinated children.

[This method of retrospective analysis is not a statistically sound procedure and is liable to give misleading results.]

J. Lorber

Venereal Diseases

1286. **A Study of the Etiology, Epidemiology, and Therapeusis of Nongonococcal Urethritis**
S. S. AMBROSE and W. W. TAYLOR. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 503–513, Nov., 1953. 4 figs.

In view of the prevalence of non-gonococcal urethritis amongst the troops engaged in the Korean conflict and of the paucity of factual information regarding the aetiology, epidemiology, and treatment of this condition a detailed study was undertaken at the Naval Field Research Laboratory and the U.S. Naval Hospital, Campe Lejeune, North Carolina, of 45 cases of non-gonococcal urethritis, 46 soldiers without infection acting as controls. The average age of the subjects was 20·8 years.

The incubation period of the disease was variable, but in over half the cases was within 10 days of the last intercourse and in four-fifths within 24 days. Some evidence of prostatitis was found in all but one case; in 31 there was clumping of the leucocytes in the prostatic secretion and in 13 others an excess of leucocytes. Examination of dark-field preparations revealed trichomonads in only one case. No intra- or extracytoplasmic inclusions consistent with the elementary bodies of the psittacosis–lymphogranuloma-venereum–trachoma group of viruses were noted. Slides stained with Giemsa stain repeatedly revealed bacteria even when none was to be seen in Gram-stained specimens. Cocco-bacillary forms about 0·5 μ long, staining red or green with Giemsa, and apparently lying in clusters within what appeared to be the cytoplasm of degenerating epithelial cells or in a small fragment of mucus were noted in one-third of the patients, but in none of the controls.

The bacterial flora was varied and abundant: bacteria obtained from the urethra, urine, or prostate were cultured before and after therapy in all cases. Gram-positive cocci were found in 36·6%, corynebacteria in 23·0%, Gram-negative bacilli in 24·2%, other Gram-positive bacilli in 9·5%, streptococci in 3·8%, and fungi in 2·6%. Neisseriae other than the gonococcus were noted in 2 cases. Very similar types of bacteria were found in the controls.

"Terramycin" (oxytetracycline) was given to 41 patients and proved effective in dealing with the urethritis, but there was no prompt effect on the prostatic inflammation with doses of 1 g. per day. With increase of the dose to 2 g. per day the diminution in the numbers of leucocytes was apparently accelerated.

R. R. Willcox

1287. **Non-specific Urethritis: some General Observations**
R. R. WILLCOX. *South African Medical Journal* [*S. Afr. med. J.*] **27**, 1132-1134, Dec. 12, 1953. 2 refs.

1288. **The Effect of Penicillin Treatment on the Microscopic Appearance of Syphilitic Aortitis**
H. A. SINCLAIRE and B. WEBSTER. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **38**, 54-56, Jan., 1954. 5 refs.

1289. **Latent Syphilis *Ignorée* and Syphilis Control during the Epidemic in Denmark, 1942 to 1949. A Statistical Analysis of Newly Diagnosed Untreated Cases**
I. B. SVENDSEN. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 553–573, Nov., 1953. 3 figs., 29 refs.

In this paper an attempt is made to evaluate statistically the efficacy of the measures adopted in Denmark to control the syphilis epidemic which occurred in 1942 by comparing the incidence of "latent syphilis *ignorée*" (previously unrecognized latent syphilis) per 1,000 persons tested serologically before and after the epidemic, the years 1939 and 1949 being chosen for survey.

Denmark would appear to provide ideal conditions for such a survey in that routine serological tests for syphilis are carried out on nearly every patient admitted to hospital, regardless of the diagnosis, and that all such tests are centralized in one laboratory at the State Serum Institute. Furthermore, the Institute publishes a monthly list of all newly diagnosed cases of syphilis, including seronegative cases notified compulsorily to the Board of Health.

The author first tabulates the total numbers of cases of primary, secondary, and latent syphilis newly diagnosed in males and females in each year from 1938 to 1949 inclusive and their distribution per 100 cases diagnosed. The latent cases are further divided into those with positive diagnostic support in the history and those without any relevant history (*ignorée*). From these uncorrected figures and those for the annual numbers of blood specimens tested it is estimated that the incidence of latent syphilis *ignorée* was 1·9 cases per 1,000 blood specimens examined in 1939 and 0·9 cases per 1,000 in 1949.

Certain corrections are then applied to the absolute number of blood specimens tested so as to exclude duplicate specimens from the same individual and specimens from blood donors, foreigners, children under 15, and pregnant women (routine testing in pregnancy having become compulsory in 1945). Similarly the absolute numbers of cases of latent syphilis diagnosed were corrected to exclude those in which the reactions proved to be non-specific. Finally, both "minimum" figures, including only those cases of latent syphilis in which there was definitely no history, and "maximum" figures, including also cases in which only one blood specimen was received and cases without any data

regarding history, were calculated for the rate of detection of latent syphilis *ignorée* for the two years.

A statistically significant fall occurred in the " maximum " detection rate of latent syphilis *ignorée* between 1939 and 1949, that for males falling from 3·0 to 1·0 per 1,000 specimens tested, and that for females from 2·2 to 1·0 per 1,000. The " minimum " rate, however, showed a significant decrease only among the males (from 1·2 to 0·7 per 1,000 specimens).

The author concludes that there are now fewer unrecognized cases of latent syphilis in Denmark than before the war and therefore that the control of syphilis during the epidemic period " must be said to have been satisfactory from the point of view of the criterion of finding the largest possible number of infected subjects as early as possible ". *Benjamin Schwartz*

1290. **A Contribution to the Investigation of Syphilis by Means of Serological Micro-tests.** (Ein Beitrag zur Luesuntersuchung mittels serologischer Mikroverfahren) R. H. LAUN and E. GEHM. *Zeitschrift für Hygiene und Infektionskrankheiten* [*Z. Hyg. InfektKr.*] **138**, 189–194, 1953. 17 refs.

At the Municipal Bacteriological Research Laboratory, Würzburg, the authors subjected 1,477 samples of serum to a battery of tests which included a micro-test for which the antigen, cardiolipin, has a similar composition to that used in the V.D.R.L. test. Comparison showed that this micro-cardiolipin test gave very satisfactory results, correctly diagnosing 91% of all positive sera, as compared with 86% by the complement-fixation test (using cardiolipin as antigen), 62% by the " citochol " reaction, 43% by a modified Meinicke test, and 27% by the original Wassermann reaction.

The authors consider that the micro-cardiolipin test is very suitable for screening purposes, because of its simplicity, the short time required for its performance, and its high degree of specificity. As only 0·03 ml. of serum is required, the test has obvious advantages when only small amounts of blood are available.

G. W. Csonka

1291. **Studies on the Comparative Behavior of Various Serologic Tests for Syphilis. III. A Report on Return to Seronegativity following Successfully Treated Primary and Secondary Syphilis**
J. C. CUTLER, B. J. CHESTER, and E. V. PRICE. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 514–528, Nov., 1953. 2 figs., 17 refs.

The cumulative percentages of sustained seronegative reactions to the Kline exclusion, Mazzini, Kline diagnostic, Kahn, Hinton, Eagle, and Kolmer tests for syphilis using crude lipoidal antigens were studied at the U.S. Public Health Service Venereal Disease Laboratory in 100 patients with primary syphilis and 100 patients with secondary syphilis, following the treatment of both groups with penicillin. At 12 months the seronegativity rates with the different tests ranged from 88·6 to 99·0% for the primary cases and from 61·2 to 86·0% for the secondary cases. At 24 months the respective figures were 88·8 to 100% and 75·2 to 98·0%, and at 36 months 92·5 to 100% and 77·9 to 100% respectively.

A more rapid return to seronegativity was noted following treatment of the cases of primary than of secondary syphilis. The Kline exclusion test, which is more sensitive than the others, was the last to become negative. In both primary and secondary syphilis the Kahn, Eagle, and Hinton tests all showed approximately the same rate and pattern of return to negativity. The Kline diagnostic test was a little slower in cases of secondary syphilis. The Kline exclusion and Mazzini tests showed slower rates of reversal, particularly in cases of secondary disease. Thus, the authors point out, in evaluating the results of treatment consideration should be given to the nature of the tests employed.

R. R. Willcox

1292. **The Mazzini Cardiolipin Microflocculation Test in the Serology of Syphilis**
H. N. BOSSAK, A. HARRIS, W. P. DUNCAN, S. OLANSKY, and B. J. CHESTER. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 536–539, Nov., 1953. 2 refs.

At the U.S. Public Health Service Venereal Disease Research Laboratory the sensitivity of the recently developed Mazzini cardiolipin microflocculation (M.C.M.) test was compared with that of 8 other serological tests for syphilis on 1,061 sera. The tests used were the V.D.R.L. slide and tube tests, the Kline standard, and the Kolmer simplified tests (all using cardiolipin–lecithin antigen) and the Mazzini lipoidal, the Kahn Standard, the Eagle flocculation, and the Hinton flocculation tests (in all of which lipoidal antigens are used).

Of the 1,061 sera, 338 were non-reactive and 462 were reactive to all 9 tests; these are not further considered, as the interest of the study lay in the remaining 261 sera in which discrepancies between the test results were found. In this group the M.C.M. test gave the highest number of positive reactions, namely, 79% of sera, and the Kahn standard test was the least reactive, giving a positive result in 35%. In relation to the clinical state of the patients, the M.C.M. test was the most reactive at all stages of syphilis, but it also gave a higher number of reactions with non-syphilitic sera than any other test in which cardiolipin was the antigen. The four tests using lipoidal antigen produced a higher number of false positive reactions than the cardiolipin-antigen tests, except for the M.C.M. test, which gave the highest rate.

Finally the incidence of " sole positive reaction " is considered. Thus the M.C.M. test was the only test to give a positive result in the presence of negative results with all the 8 other tests in 25 cases, in 18 of which the serum was known to be syphilitic. At the other end of the scale the Kahn standard test was the only test to give any reaction in 5 cases, all in the non-syphilitic category. The Kline standard, the V.D.R.L. slide and tube tests, and the Hinton flocculation test never gave a sole positive reaction, but the reaction, if positive, was always corroborated by a positive reaction from at least one other test. *Ferdinand Hillman*

Tropical Medicine

1293. **Plasma Protein Concentration of Normal Adults Living in Singapore**
G. R. WADSWORTH and C. J. OLIVEIRO. *British Medical Journal* [*Brit. med. J.*] **2**, 1138–1139, Nov. 21, 1953, 12 refs.

The investigation described in this paper from the University of Malaya, Singapore, was undertaken to determine whether there was any difference in plasma protein concentration between subjects of European and Asian stock, and whether the concentration in healthy subjects was the same in the tropics as in a temperate climate. The total plasma protein concentration was estimated by the copper sulphate specific gravity method in 80 men and 59 women living under good conditions in Singapore. About one-third of the subjects were of Asian and two-thirds of European stock. In 25 cases the plasma protein concentration was also estimated by the macro-Kjeldahl method, the results agreeing closely with those obtained by the copper sulphate specific gravity method. No significant difference was observed in the total plasma protein concentration between men and women or between subjects of Asian and European stock, the mean level of all samples being 7·7 g. per 100 ml. (S.D. 1·31). The authors consider that this level is relatively high, and suggest that it may be due to a compensatory change to prevent an excessive loss of fluid from the blood into the tissue spaces in subjects living in the tropics. Haemoconcentration as a factor was excluded. *J. Lorber*

1294. **The Toxicity of Chloroquine in Hepatic Amoebiasis in Africans**
J. WILKINSON. *East African Medical Journal* [*E. Afr. med. J.*] **30**, 403–415, Oct., 1953. 17 refs.

It has been shown that chloroquine in the dosages usually employed for the treatment of malaria has negligible toxic effects. The present author describes the effects observed with larger doses in the treatment of hepatic amoebiasis in 112 Kikuyu tribesmen of all ages. A dose of 600 mg. of chloroquine sulphate was given daily for two weeks to 92 of the patients, the remaining 20 receiving twice the dose of chloroquine for one week only. All the patients were given a daily dose of 1,890 mg. of di-iodohydroxyquinoline concurrently.

Toxic reactions were observed in 52 of the patients; headache was the most frequent manifestation, but giddiness, nausea, anorexia, and vomiting were common. Blurred vision and rashes were noted in a few cases. Most of the patients lost weight, the average loss being 2 lb. (1 kg.). The author states that the incidence of toxic effects was much higher than that found by Conan in a series of cases of extra-intestinal amoebiasis (*Amer. J. trop. Med.*, 1948, **28**, 107; *Abstracts of World Medicine*, 1948, **4**, 332). Toxic reactions were more severe, though not more frequent, in patients receiving the double dose of chloroquine, and females were more often affected than males. No relationship between age and toxicity was observed. None of the toxic effects was permanent, and there were no deaths.

The author suggests that the high incidence of toxic reactions is due to the poor physique of the Bantu, and that chloroquine is a valuable and fairly safe schizontocide. *H. David Friedberg*

1295. **Tuberculosis in Nigeria**
E. H. BRAUN. *Tubercle* [*Tubercle* (*Lond.*)] **34**, 301–307, Nov., 1953. 7 refs.

Examination of the findings in a total of 5,429 necropsies carried out at Lagos, West Africa, between 1945 and 1952 inclusive showed that death was due to tuberculosis in 640 cases. The most striking feature of the series was the presence of enlarged caseous lymph nodes in all the subjects (310) under 16 years of age and in 210 of 330 subjects over this age. In the latter group the picture was that of the so-called childhood type of tuberculosis, namely, rapidly progressive caseation with little fibrosis and a tendency to widespread dissemination.

The abdominal lymph nodes were involved in 337 of the 640 cases. This is taken as suggesting that the mouth is the usual portal of infection in the Nigerian, to be accounted for by the native's habit of eating with the hands. Bone and joint lesions were rare.

Compared with the European, the Nigerian has a higher degree of hypersensitivity and a lower degree of immunity. The author suggests that the Nigerian may respond well to administration of antibiotics, in which case the relative lack of fibrosis may not be a disadvantage. *D. Weitzman*

1296. **Control of Vomiting in Cholera and Oral Replacement of Fluid**
H. N. CHATTERJEE. *Lancet* [*Lancet*] **2**, 1063, Nov. 21, 1953. 3 refs.

Vomiting is a major alimentary symptom in cholera, leading rapidly to exhaustion and shock. In this paper from the Chittaranjan Hospital, Calcutta, the author describes the treatment of vomiting in 186 cases of cholera by oral administration of tablets containing 25 mg. of "avomine" (promethazine 8-chlorotheophyllinate). In mild cases (33) vomiting was often relieved by administration of a single tablet; when, however, vomiting continued further tablets were given, the largest dose being 6 tablets in 24 hours in one case. In all the cases vomiting was ultimately controlled by avomine. No toxic reactions were observed. The drug had no effect on the diarrhoea, but the control of vomiting made it possible to treat dehydration by administration of fluids by mouth. *V. J. Woolley*

Allergy

1297. **An Evaluation of Treatment of Ragweed-sensitive Patients with Adrenocorticotropic Hormone in Gelatin**
J. Roy, R. A. Cooke, and W. B. Sherman. *Journal of Allergy* [*J. Allergy*] **24**, 506–509, Nov., 1953. 2 refs.

At the Institute of Allergy, Roosevelt Hospital, New York, 20 patients with ragweed hay-fever, with or without asthma, were treated during the ragweed season with 40 units of ACTH gel daily for periods varying from 2 to 19 days. There was marked improvement in all patients within 48 hours, and the majority were symptom-free after 4 or 5 injections. Two patients with hay-fever who had become free of symptoms after 2 and 3 injections respectively during the height of the season remained free during the remainder of the ragweed season without any further treatment. *H. Herxheimer*

1298. **Significance of Changes in the Expiratory Rate Observed during Measurement of the Vital Capacity in Asthma**
F. C. Lowell and I. W. Schiller. *Journal of Allergy* [*J. Allergy*] **24**, 492–498, Nov., 1953. 4 figs., 4 refs.

The changes in the rate of expiration of patients with genuine or induced attacks of asthma were studied at the Evans Memorial Hospital (Boston University School of Medicine). Expiration with maximal effort was traced from the moment of maximum inspiration on the drum of a spirometer moving at 0·56 cm. per second, and the logarithm of the volume of air remaining to be expired was plotted against the time. It was shown that usually the slowing down of the expiratory flow occurs at a constant rate, but in some cases the rate of flow changes in an unpredictable and unexplained way. The so-called timed vital capacity and indices derived from it do not represent the manner in which air is expelled from the lungs, but the procedure described does so accurately. *H. Herxheimer*

1299. **Bronchostenosis Complicating Asthma**
T. W. Mears, L. E. Prickman, and H. J. Moersch. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **152**, 997–1000, July 11, 1953. 2 figs., 9 refs.

During the 10-year period 1941–50 at the Mayo Clinic 1,034 asthmatic patients underwent bronchoscopy, 327 of whom were found to have benign stenosis of an inflammatory nature in one or more bronchi. The majority of the strictures occurred in the major bronchi below the orifice of the upper-lobe bronchus [no other pathological feature is mentioned].

The clinical picture was considered typical, there being retention of secretion with cough and fever, infected sputum, and often localized physical signs such as wheezing, with emphysema, pneumonitis, and bronchial occlusion.

The authors advise aspiration and dilatation with forceps when bronchoscopy reveals a stricture; 60·5% of the patients in their series obtained immediate relief from this procedure. [This does not compare very favourably with the control group, in which 55% obtained immediate relief, but the long-term results are considered to be superior. Not all would agree that asthmatic patients rarely object to bronchoscopy. No clear explanation of the pathological basis is given.] *K. Gurling*

1300. **Adenotonsillectomy and its Relation to Asthma**
G. Sobel. *Annals of Allergy* [*Ann. Allergy*] **11**, 583–589, Sept.–Oct., 1953. 3 figs., 8 refs.

At the Rockville Center, New York, 100 patients suffering from infectious asthma or from a combination of infectious asthma and allergic asthma were studied. In 68 cases the patients' tonsils and adenoids had been removed before anti-allergic treatment was instituted, 40 of these patients having developed asthma for the first time after the operation—11 of them within the first year and another 15 within the following 3 years. Of the 28 patients who had asthma before the operation, in 23 the asthma recurred within one year. It is concluded that tonsillectomy is too often carried out because allergic vasomotor rhinitis is confused with recurrent colds or in the hope of relieving allergic asthma, but there is no evidence that the presence or absence of tonsils and adenoids is related to the severity of asthma. *H. Herxheimer*

1301. **The Absence of Histamine-fixing Properties from the Serum of Allergic Subjects.** (Le pouvoir histaminopexique du sérum sanguin. Son absence chez les sujets allergiques)
J. L. Parrot and C. Laborde. *Presse médicale* [*Presse méd.*] **61**, 1267–1269, Oct. 7, 1953. 5 refs.

The authors have investigated the ability of serum from normal and allergic subjects to fix histamine. They had previously shown that the injection of normal human serum into guinea-pigs conferred some protection against histamine, whereas serum from allergic subjects gave no protection. In the present study, histamine dihydrochloride was added to a 1-in-20 dilution of serum. "Normal" serum fixed about 33% of the histamine, and this figure was taken as a measure of normal histamine-fixing power. It was found that the histamine was taken up by the gamma-globulin fraction, and that where this did not occur, a diffusible inhibiting substance was present. Histamine fixation took place in the serum of 121 normal subjects and to a somewhat lesser degree in 70 subjects suffering from a variety of non-allergic disorders, but there was no, or greatly reduced, fixation in the serum of 174 (94%) out of 185 allergic subjects. (The authors include among allergic disorders, asthma, urticaria, eczema, migraine, rheumatic fever, chronic rheumatism, periarteritis nodosa, tuberculosis, and gastric and duodenal ulcer.)

The failure to fix histamine in the allergic patients persisted during symptom-free periods and was not

associated with any abnormality of serum globulin, since in sera which failed to fix histamine the isolated globulin could not do so after separation by ammonium sulphate precipitation. The addition of histamine itself to the serum prevented further histamine from being fixed, but on dialysis of the serum the histamine disappeared rapidly, whereas the inhibiting substance disappeared far more slowly, thus indicating that the inhibiting substance was not histamine. The suggestion is made that the allergic tendency of certain subjects may be due to the presence of this inhibiting substance, and that a serum test of this type could be used as a general test for allergic constitution.

[Although it is unlikely that many workers would accept the very wide definition of allergic conditions adopted by the authors, their finding is of interest and might be worth further study.] *J. Pepys*

1302. **Antibody Formation in Allergic and in Normal People**
D. D. ADAMS. *Lancet* [*Lancet*] **2**, 911–912, Oct. 31, 1953. 1 fig., 2 refs.

The author suggests that allergic subjects may produce antibody more readily than " normal " subjects. In this study, carried out at Otago University Medical School, Dunedin, the antibody formed in response to injection of typhoid–paratyphoid (T.A.B.) vaccine was measured in two groups of students to test this theory. The allergic group consisted of 11 students, of whom 5 suffered from chronic asthma, 5 from hay-fever, and one from eczema, while the normal group was composed of 10 students with no personal or family history of allergy. Subcutaneous injections of 0·25 ml. of T.A.B. vaccine, followed by 0·5 ml. 2 weeks later, were made into each subject. Agglutination tests were carried out at 1, 2, 3, and 5 weeks after the first injection.

The average response of the " allergic " group was considerably higher than that of the " normal " group. Statistical analysis showed that the chance of such a difference occurring as a result of random variation was about 1 in 20 ($P=0·05$). It is suggested that this abnormally sensitive response of antibody formation in allergic subjects may be responsible, in part at least, for some of their symptoms. *R. S. Bruce Pearson*

1303. **Hypersensitivity to Bee Sting. Report of a Fatal Case and Review of Literature**
J. R. SCHENKEN, J. TAMISIEA, and F. D. WINTER. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **23**, 1216–1221, Dec., 1953. 1 fig., 22 refs.

The authors record the case of a man of 21 who was known to be sensitive to bee stings, and who died from anaphylactic shock half an hour after he had been stung. Post-mortem examination showed the presence of tenacious mucus in the respiratory tract; the epiglottal folds and the vocal cords were oedematous, and the cerebral convolutions of the brain were also flattened as the result of oedema.

The authors review the literature on bee-sting hypersensitivity, analyse the symptoms and post-mortem findings in 10 cases and discuss the treatment.

[In the recommendation that " adrenalin (1:1,000) should be given slowly in doses of 0·5 ml. intravenously as often as necessary to counteract any shock that might be present " the word " intravenously " has presumably been printed in error. Subcutaneous injection in this dosage is reasonable and can be carried out by the patient himself. To administer adrenaline intravenously in the dose suggested would be a highly dangerous proceeding.] *R. S. Bruce Pearson*

1304. **Food Allergy in Infants, with Special Reference to Allergy to Cow's Milk.** (Nahrungsmittelallergie, insbesondere Kuhmilchallergie bei Säuglingen)
M. VEST. *Annales paediatrici* [*Ann. paediat.* (*Basel*)] **181**, 277–294, Nov., 1953. 2 figs., bibliography.

A study was made at the Children's Hospital, Basle, of 9 babies who were allergic to cow's milk and one with allergy to bananas. Scratch tests and intradermal tests with food extracts, as well as the Prausnitz–Kuester test, were considered to give unreliable results, and therefore estimation of the " leucopenic index " as proposed by Vaughan (*J. Allergy*, 1934, **5**, 601) was introduced as a diagnostic aid. Shortly after feeding the allergenic foods, a decrease in the leucocyte count took place; this was followed in most cases by an increase lasting several hours, due to the appearance of juvenile forms and of a larger number of neutrophil and eosinophil leucocytes. In spite of these observations the author issues a warning against considering the leucopenic index test as complete evidence of food allergy.

The allergic reaction of the infants to cow's milk mostly disappeared spontaneously. During the allergic phase milk from no other animal was tolerated, and human milk had to be given. As an alternative to milk a 10% watery solution of soya bean flour with 5% of sugar was satisfactory. However, in one infant allergy to soya bean developed, and it was necessary to feed this child on nut meal, oatmeal, and wheat germ, with added calcium and vitamins. *Kate Maunsell*

1305. **Complement-fixing Antibodies against Foodstuffs in Children.** (Komplementbindende Antikörper gegen Nahrungsmittel bei Kindern)
E. BERGER. *Annales paediatrici* [*Ann. paediat.* (*Basel*)] **181**, 295–305, Nov., 1953. 4 refs.

The author confirms the passage of antigens of milk, soya bean, and oats from the intestine of children into the blood circulation. Complement-fixing antibodies were demonstrated in the blood serum of 20 out of 84 children examined at the Children's Hospital, Basle. Positive reactions were obtained with high antigen dilutions as well as with concentrated solutions. In many of the cases the degree of antibody formation did not run parallel with the clinical symptoms. In one patient allergic to cow's milk, repeated complement-fixation tests were carried out. The complement-fixing antibodies disappeared with clinical improvement. The possible value of estimation of complement-fixing antibodies in the diagnosis of allergic conditions is discussed. *Kate Maunsell*

Nutrition and Metabolism

1306. **Some Observations on the Use of Fructose and Invert Sugar in Infants**
R. M. TODD. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **46**, 1066–1068, Dec., 1953. 2 figs., 4 refs.

At Alder Hey Children's Hospital, Liverpool, the author has investigated the possible value of invert sugar in place of glucose in intravenous infusions given to children suffering from gastro-enteritis. An initial investigation was made on healthy convalescent infants aged 3 to 6 months. After 5 days on normal diet, they were given by intravenous infusion or orally 20 ml. per lb. (44 ml. per kg.) body weight of a 5%, 7·5%, or 10% solution of either glucose or fructose, or of a 10% solution of "invose", a proprietary brand of invert sugar. The blood sugar level was then estimated hourly and the urine examined every 2 hours. The total blood sugar level after the infusion of fructose or invose was lower than that after infusion of glucose, and no sugar was excreted in the urine.

The method was then applied to the study of 34 infants suffering from gastro-enteritis. The children received the usual standard regimen of treatment used in the hospital in regard to electrolyte intake and regrading of milk feeds, but alternate patients were given 10% solutions of invert sugar instead of 5% glucose, in milder cases by mouth and in severe cases intravenously. Progress, judged by the disappearance of diarrhoea and clinical signs, was equally satisfactory in the two groups. There were no cases of venous thrombosis from the high concentration of invert sugar in the solution infused, nor was the renal threshold reached. The author suggests that this investigation points to the possible value of giving invert sugar as an alternative to glucose to children suffering from conditions in which intravenous therapy may be required for several days and in which a high caloric intake without an increase in fluid volume is advantageous. The method might also be of value in certain surgical conditions. *E. H. Johnson*

1307. **Relationship of Adiposity to Serum Cholesterol and Lipoprotein Levels and Their Modification by Dietary Means**
W. J. WALKER. *Annals of Internal Medicine* [*Ann. intern. Med.*] **39**, 705–716, Oct., 1953. 4 figs., 23 refs.

The influence of weight loss on the serum level of cholesterol and of lipoproteins was studied in 39 outpatients (11 women and 28 men), aged 29 to 68 years, at the Peter Bent Brigham Hospital, Boston. The initial weight of the patients varied from the ideal to 50% above the ideal as defined in Metropolitan Life Insurance height–weight tables. None of the patients was in congestive heart failure, but 29 had definite cardiovascular disease. The patients were given a diet which provided 100 g. of protein, 20 g. of fat, and 100 g. of carbohydrate, and included 2 eggs daily, equal to about 600 mg. of cholesterol. Most of them lost weight rapidly during the period of observation, the average loss per week being 1·6 lb. (724 g.) and the total loss varying between 7 and 40 lb. (3 and 18 kg.). This was accompanied by a statistically significant reduction in the serum level of all three categories of lipoproteins, especially of the Sf 12–20 fraction, but not by a comparable fall in the serum cholesterol level. No change was observed in the serum lipoprotein level when the eggs were abruptly withdrawn from the diet. Apparently dietary fat may affect cholesterol absorption and re-absorption from the colon, since during periods of rapid reduction in weight, when large amounts of endogenous fat are metabolized, the serum lipoprotein was often at its lowest. On the other hand forced feeding of 2 healthy subjects with a diet containing less than 15 g. of fat and 50 mg. of cholesterol daily resulted in an increase in weight of 10 lb. (4·5 kg.) in 10 days; the rise in the serum cholesterol level was slow and delayed, but a threefold increase in the level of the Sf 12–20 fraction of the lipoproteins with an even greater increase in the Sf 35–100 fraction was observed. These levels fell abruptly on termination of the forced feeding.

It is concluded that the rise in the serum lipoprotein level is to be attributed to non-fat calories.

L. H. Worth

1308. **Effect of Added Vitamin D on the Calcium Balance in Elderly Males**
P. G. ACKERMANN and G. TORO. *Journal of Gerontology* [*J. Geront.*] **8**, 451–457, Oct., 1953. 15 refs.

In a previous investigation the authors found that the calcium requirement of elderly men was higher than that of young adults (*J. Geront.*, 1953, **8**, 289; *Abstracts of World Medicine*, 1954, **15**, 32). Since then they have studied the effect of administration of vitamin D on the calcium and phosphorus requirements of 6 of the same subjects. All the subjects were in negative calcium balance during an initial period of 60 days on a normal diet. The addition to the diet of 25,000 I.U. of vitamin D per day resulted in an increase in calcium retention of 5 mg. per kg. body weight per day in 5 subjects and of 10 mg. per kg. in one subject. The average phosphorus balance was unchanged. With doses of 600 or 1,800 I.U. per day the increase in calcium retention varied from 1 to 3 mg. per kg. per day. The flame-photometer method was used to determine the calcium balance. [The original paper should be consulted for the detailed description of this method.] *F. W. Chattaway*

1309. **Cation Exchange Resins: a Clinical and Biochemical Study of Their Use in Oedema**
H. D. BREIDAHL. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] **2**, 186-194, Nov., 1953. 1 fig., 19 refs.

See also Cardiovascular System, Abstract 1327

Gastroenterology

STOMACH AND DUODENUM

1310. **The Clinical Value of Gastro-intestinal Cytologic Diagnosis**

C. E. RUBIN, B. W. MASSEY, J. B. KIRSNER, W. L. PALMER, and D. D. STONECYPHER. *Gastroenterology* [*Gastroenterology*] **25**, 119–138, Oct., 1953. 15 figs., 47 refs.

The technical requirements for successful cytological examination of the gastro-intestinal tract and the value of this procedure in the diagnosis of carcinoma are discussed. The authors first point out that cytological examination of the digestive tract calls for meticulous preparation of the patient and skilful use of improved methods of cell collection. They then describe the methods they found most useful in 300 patients at the Frank Billings Medical Clinic (University of Chicago). For the oesophagus a Levin tube is passed to the level of the lesion; this is followed by vigorous lavage and aspiration. The aspirate is stored in an ice bath for not more than 15 minutes and then layered over serum, centrifuged, and the deposit fixed in an ether–ethanol mixture. For the stomach the antral abrasive-balloon technique followed by chymotrypsin lavage has, in the authors' experience, given the best results. The deflated balloon, which has a mercury weight at the tip, is passed into the duodenum by gravity with the patient in the right lateral decubitus position; then, with the patient in the upright position, the balloon is partially inflated, causing its abrasive net to ride back into the stomach and abrade any antral lesion. Before specimens are obtained from the colon the patient is given castor oil and a tap-water enema. One litre or more of Ringer's solution is then introduced and dispersed throughout the colon by varying the position of the patient and by massage. The return is collected by gravity drainage and massage; 10 drops of ovalbumen are added to each 100 ml. of solution, and the whole is centrifuged and fixed in the usual way.

Illustrative case histories are given. It is concluded that by cytological examination it is possible to differentiate more precisely between benign and malignant lesions.

[Those interested should consult the original paper, because details of many other techniques are given.]

J. Naish

1311. **Growth of *Clostridium welchii* in the Stomach after Partial Gastrectomy**

J. W. HOWIE, I. B. R. DUNCAN, and L. M. MACKIE. *Lancet* [*Lancet*] **2**, 1018–1021, Nov. 14, 1953. 16 refs.

During the first week after partial gastrectomy diarrhoea is usually mild, but occasionally, severe diarrhoea develops on the 3rd or 4th postoperative day. Examination of the stools in these cases generally fails to reveal any specific intestinal pathogenic organisms.

In 12 out of 15 patients who had undergone partial gastrectomy at the Western Infirmary, Glasgow, however, *Clostridium welchii* was found in considerable numbers in the stomach contents, and in 8 cases also detectable quantities of toxin, suggesting that the organism was resident in the stomach and not merely transient. Only one of these 15 patients developed diarrhoea following the operation, and in this case there was no more toxin in the stomach than in the other cases. It is, however, probable that the development of diarrhoea would depend more on the concentration of organisms and toxins in the ileum than that in the stomach. The authors conclude that the evidence suggests that further research is required.

Norman C. Tanner

1312. **Carcinoma of the Stomach. A Review of 161 Cases Treated at the New Haven Hospital from January, 1941, to December, 1946, and a Comparison with Two Previous Series, 1920–1930 and 1931–1940**

P. SAFAR and E. E. CLIFFTON. *Cancer* [*Cancer* (*N.Y.*)] **6**, 1165–1173, Nov., 1953. 26 refs.

The results of treatment in 158 cases of carcinoma of the stomach admitted to New Haven Hospital (Yale University) between 1941 and 1946 are compared with those obtained in two earlier series treated at the same hospital during the years 1920–30 and 1931–40. In 46 of the 158 cases the condition was inoperable or the patient refused operation; in 44 exploration only was carried out; and in 12 palliative procedures, such as gastrostomy and jejunostomy, were performed. The average survival period of the patients in these three groups did not exceed 10 months. Of the 56 patients subjected to gastric resection, 14 survived 5 years, and the 5-year survival rate for the whole series was thus 8·8%, compared with 2·5% and 4·8% in the two earlier series respectively.

The authors believe that this improvement in the 5-year survival rate is not related to earlier diagnosis or earlier treatment, but to the fact that operative mortality is lower and resectability rate higher. Better results were obtained in cases of fundal growth than in cases of prepyloric carcinoma. Eight of the patients are known to have survived for more than 10 years.

K. Whittle Martin

1313. **Application of Balloon Technique in Detection of Cancer**

D. L. S. CHAPMAN, C. T. KLOPP, and L. I. PLATT. *Cancer* [*Cancer* (*N.Y.*)] **6**, 1174–1176, Nov., 1953. 2 figs., 3 refs.

The abrasive-balloon method of obtaining specimens of stomach contents for cytological examination, as described by Cooper (*J. Amer. med. Ass.*, 1952, **150**, 688), was tried at the George Washington University Cancer Clinic, Washington, D.C., on 65 patients with mild gastro-intestinal symptoms, but without gastric

carcinoma; only 45 completed the test. The specimens obtained were satisfactory from the cytologist's point of view; nevertheless, the method was disappointing because one-third of the patients were unwilling or unable to swallow the tube and the time required to complete the test was considerable. The authors conclude that the abrasive-balloon technique is too time-consuming " for use in routine cancer-detection examination ".

K. Whittle Martin

1314. **A New Rapid Method for Stomach-cancer Diagnosis: the Gastric Brush**

J. E. AYRE and B. G. OREN. *Cancer* [*Cancer (N.Y.)*] **6**, 1177–1181, Nov., 1953. 7 figs., 3 refs.

The low calcium content of malignant cells is apparently responsible for the tendency of malignant epithelial cells to separate more readily than normal epithelial cells. In view of this tendency the authors devised a rotating gastric brush for the collection of fresh cytological specimens from the stomach. The brush, which is in a sleeve, is easily passed into the empty stomach, and is pushed out of the sleeve once the pyloric region is reached. Light contact of the brush with a tumour removes large numbers of malignant cells, while contact with normal tissue yields few benign cells. The cellular material is expressed from the brush immediately after withdrawal and smears prepared at once.

While it is too early to assess the degree of accuracy to be obtained with this method the authors believe that by its use carcinoma of the stomach, may be diagnosed " at a more favourable stage " than is possible with most existing methods.

K. Whittle Martin

1315. **The Neurovascular Mechanism of Gastric Ulcer Formation. A Comparative Study**

H. B. BENJAMIN. *Journal of the International College of Surgeons* [*J. int. Coll. Surg.*] **20**, 327–337, Sept., 1953. 6 figs., 24 refs.

The vascular pattern of the stomach was investigated in 100 human surgical or post-mortem specimens and in experiments on 150 dogs at Marquette University School of Medicine, Milwaukee, by the intra-arterial injection of a contrast material consisting of 20% colloidal silver iodide and 10% bismuth oxychloride, followed by radiological and histological examination of the specimen. The experiments on dogs were carried out under anaesthesia in the living animal. The contrast medium was injected into the right gastric and gastro-epiploic arteries in the human specimens, since visualization of the antrum only was required, and into the descending thoracic aorta in the dogs. In certain of the animal experiments the stump of the left or right vagus nerve was stimulated during the injection.

It was found on the one hand that the vascular pattern in the healthy human stomach corresponded to that found in the unstimulated stomach of the dog, and on the other that the pattern found in the human stomach in cases of gastric ulcer was identical with that found in dogs in which the stump of the right vagus nerve had been stimulated. Stimulation of the left vagal stump led to a diminished vascular supply to the area of the cardia and fundus. Stimulation of the right vagal stump caused the complete disappearance of visualization of the vessels in the region of the *Magenstrasse*.

These observations led the author to the conclusion that regional ischaemia produced by the hyperactivity of the vagus is the primary cause of peptic ulceration, and he associates himself with Necheles in rejecting the acid theory of the pathogenesis of peptic ulcer.

R. Schneider

1316. **An Evaluation of " Prantal " in Ulcer Management. Follow-up of Preliminary Report**

T. S. HEINEKEN. *Review of Gastroenterology* [*Rev. Gastroent.*] **20**, 829–39, Nov., 1953. 14 figs., 12 refs.

The results of a preliminary trial of " prantal " (a quaternary ammonium (piperidylidene) derivative) in 26 cases of peptic ulcer (*Amer. Practit.* (*Philad.*), 1952, **3**, 701) were so encouraging that the series was extended to a total of 107 cases (93 of duodenal and 14 of gastric ulcer). Prantal is a cholinergic blocking agent which reduces gastric motility and secretion, including histamine-induced secretion. Other atropine-like effects, such as mydriasis and dryness of the mouth, occur to a much less extent with prantal than with many other drugs having a similar action.

The average age of the patients was 45 years, and symptoms had been present for periods varying from a few weeks to 30 years. All the patients received a daily dose of 50 to 200 mg. of prantal, but 20 were not restricted as to diet, 20 had a bland diet, and the remaining 67 had an ulcer diet with antacids. [The series was uncontrolled.] Signs and symptoms recurred in only 8 patients, and these cleared when further prantal was given. Only 4 patients did not obtain complete relief from pain while taking the drug. There were no side-effects of sufficient severity to cause treatment to be discontinued.

[In peptic ulcer, for which so many therapeutic panaceas have been suggested in the past, a thoroughly controlled therapeutic trial is essential before too much reliance is placed on any given agent. However, these results seem to be very striking and certainly indicate the urgent need for a controlled trial of prantal.]

G. A. Smart

1317. **Autopsy Survey of Peptic Ulcer Associated with Other Disease. A Review of Related Etiological Factors Concerned**

F. B. MEARS. *Surgery* [*Surgery*] **34**, 640–654, Oct., 1953. Bibliography.

In view of the many different theories concerning the aetiology of peptic ulcer and, in particular, the possibility that vascular factors may play a part, the author investigated the incidence post mortem of peptic ulceration as a complication of other diseases.

A review of the findings in 1,000 consecutive necropsies carried out at the University of Minnesota, Minneapolis, during 1942 revealed that there were 32 cases in which gastro-duodenal erosion or ulcer, though present, was not the primary cause of death. [The incidence of scars is not mentioned.] In 11 of these 32 the primary diag-

nosis was coronary occlusion, hypertensive heart disease, or generalized arteriosclerosis. To determine the significance of this finding the necropsy records in 168 consecutive cases in which death was due to coronary occlusion and 116 in which the cause was hypertensive heart disease were examined; the incidence of peptic ulceration in the two groups was 7·7% and 4·3% respectively. In a number of instances the ulcers were multiple and acute.

A similar investigation in cases in which death was due to burns, fracture, or ulcerative colitis revealed peptic ulceration in 3·8% of the cases of burns (this is considered to be higher than expected, since the majority of the patients were children), 2·2% of the cases of fracture (fat embolism is thought to be significant in these cases), and 4·3% of the cases of ulcerative colitis.

[It is very difficult to assess the significance of these figures as the composition of the groups must have varied greatly as regards age and sex of the patients; it is impossible to calculate the expected incidence if there was no relationship other than chance between the various diseases and peptic ulceration.] *T. D. Kellock*

1318. **Prolonged Drug Therapy in Peptic Ulcer. I. An Evaluation of Banthine as an Adjunct to Conventional Ulcer Therapy**
E. C. Texter, C. W. Legerton, J. M. Ruffin, J. S. Atwater, D. Cayer, F. D. Cheney, R. A. Jackson, B. G. Oren, and J. M. Rumball. *Southern Medical Journal* [*Sth. med. J. (Bgham, Ala.)*] **46**, 1062–1069, Nov., 1953. 6 figs., 15 refs.

Methantheline bromide (" banthine ") was tried in the treatment of proven cases of duodenal ulcer at seven different centres in the U.S. Of a total of 250 patients, 131 received 50 mg. of methantheline 4 times a day and 119 received 0·2 mg. of atropine sulphate 4 times a day. All the patients were given the conventional bland diet with antacids and were followed up for an average of 13 months. Nine patients had to discontinue taking methantheline because of side-effects.

The patients were classified according to the results of treatment as " symptom-free", " markedly improved ", " moderately improved ", " slightly improved ", " unchanged ", or " worse ". One of the following was considered to indicate a recurrence: (1) return of dyspepsia for 5 consecutive days; (2) haemorrhage or perforation; or (3) radiological evidence of ulcer activity.

There was no recurrence in 32 of the patients receiving methantheline compared with 12 of those receiving atropine. Patients with a mild degree of ulceration responded " much better " to methantheline than to atropine, and those with a moderate degree responded " slightly better " to methantheline than to atropine; in severe cases there was little difference between the two groups in the response to either drug. Complications occurred as frequently in both groups, and the authors conclude that although symptomatic improvement can be expected with methantheline, the course of the disease is not significantly altered. *I. McLean-Baird*

See also Pathology, Abstract 1224.

LIVER

1319. **Control of Ascites in Hepatic Cirrhosis**
M. Atkinson, A. Paton, S. Sherlock. *Lancet* [*Lancet*] **1**, 128–131, Jan. 16, 1954. 4 figs., 11 refs.

The treatment of 3 cases of intractable ascites due to cirrhosis of the liver is described in this paper from the Postgraduate Medical School of London. In each case the accumulation of fluid within the peritoneal cavity was controlled by administration of a low-sodium diet (0·5 g. daily) together with mercurial diuretics, ammonium chloride, and salt-free protein supplements. The patients lost weight and the volume of ascitic fluid diminished. As paracentesis was unnecessary less protein was lost and the serum albumin level rose. It is suggested that after several months of treatment the plasma colloid osmotic pressure may rise to a level at which sodium restriction is no longer necessary. *P. C. Reynell*

1320. **Relation of Acute Changes in Colloidal Osmotic Pressure to Body Weight in Patients with Hepatic Cirrhosis and Ascites**
M. M. Best and J. D. Wathen. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **42**, 688–692, Nov., 1953. 4 figs., 18 refs.

At the University of Louisville (Kentucky) School of Medicine, 9 patients with ascites, oedema, and histologically-proved portal cirrhosis were studied before, during, and after administration of a cation–anion-exchange resin (" carbo-resin "). The clinical effects have been reported elsewhere (*J. Lab. clin. Med.*, 1953, **42**, 518). Determinations of body weight and of serum protein levels were made at intervals of 1 to 3 weeks.

The regression equations calculated for these findings showed no correlation between the changes in oedema, as determined by body-weight changes, and the changes in colloidal osmotic pressure or serum albumin level. It is considered likely, therefore, that factors other than changes in the serum protein content are responsible for the short-term accumulation or dissipation of ascites and oedema in such patients; the elimination of oedema and ascites produced by administration of resin suggests that one such factor is electrolyte balance. The long-term rise of serum protein level and colloidal osmotic pressure, which took place gradually in all patients during the treatment, is explained on the basis of improved nutritional state and greater activity of the patient after the disappearance of oedema and ascites.

Joseph Parness

1321. **On Correlations between Portal Venous Pressure and the Size and Extent of Esophageal Varices in Portal Cirrhosis**
E. D. Palmer. *Annals of Surgery* [*Ann. Surg.*] **138**, 741–744, Nov., 1953. 1 fig., 2 refs.

At the Walter Reed Army Hospital, Washington, D.C., an attempt was made to correlate the extent and severity of oesophageal varices with the portal venous pressure in 25 cases of portal cirrhosis. Liver biopsy was used to prove the diagnosis of hepatic cirrhosis in

each case. Oesophagoscopy was performed with the patient in the fasting state, and the varices classified according to the length of oesophagus involved and the external diameter of the vessels, which was measured with a small scale passed down the oesophagoscope. The portal venous pressure was measured by inserting a needle into a large varix at oesophagoscopy.

In general the most severe and extensive varices were associated with the highest portal pressures, but the relationship was not very close. Repeated examinations revealed considerable fluctuations both in the size of the varices and in the portal venous pressure in individual patients. It is concluded that the size of the oesophageal varices cannot be relied upon as an index of portal venous pressure. *D. W. Barritt*

1322. **On the Natural History of Esophageal Varices Secondary to Portal Cirrhosis. I. Observations on Spontaneous Changes in the Severity of Varices over Short Intervals (Less than One Year).** [In English]
E. D. PALMER and I. B. BRICK. *Gastroenterologia* [*Gastroenterologia (Basel)*] **80**, 257–262, Nov., 1953.

The authors here report a study of the short-term changes in extent and severity occurring in oesophageal varices due to portal cirrhosis [see Abstract 1321] in 31 patients who had not been subjected to surgical intervention. In each case oesophagoscopy was performed and the extent and size of the varicosities measured on two separate occasions. In 11 cases the interval between the two examinations was 1 to 2 weeks, and in all it was less than one year. There was an increase in the extent or the size of the varicosities, or both, in 12 of the 31, and a decrease in 4. In the remainder the condition was unchanged. In one patient varicosities covering two-thirds of the length of the oesophagus disappeared within a week, while a similar result was seen after longer periods in 3 others. There was no correlation between the clinical and laboratory evidence of the state of the liver and the extent and severity of the varices.

The authors stress the danger of making a false oesophagoscopic estimate of the severity of oesophageal varices if only one observation is made.

D. W. Barritt

1323. **The Intrahepatic Distribution of the Hepatic Artery in Man**
J. E. HEALEY, P. C. SCHROY, and R. J. SORENSEN. *Journal of the International College of Surgeons* [*J. int. Coll. Surg.*] **20**, 133–148, Aug., 1953. 9 figs., 12 refs.

Livers obtained from adult subjects at necropsy were studied by the authors at the Jefferson Medical College of Philadelphia. The biliary and arterial systems were injected with a solution of vinyl acetate in acetone, mercury sulphide being added to the solution for arterial injection making the material red in colour and opaque to *x* rays. After radiographs had been taken and the plastic allowed to harden, the parenchyma was dissolved by immersion of the organ in concentrated hydrochloric acid and the vinyl casts examined.

In all, 70 specimens were examined. In 40 there was a single hepatic artery and in the remainder the arterial supply was multiple. The intrahepatic arterial pattern was segmental and closely followed that of the bile ducts. " Accessory " hepatic arteries were proved to be aberrant segmental vessels. No evidence of gross intersegmental arterial anastomosis was found, although in some specimens extrahepatic and subcapsular anastomotic vessels connected the right and left branches of the hepatic artery. *B. G. Maegraith*

INTESTINES

1324. **Necrotising Enteritis Following Gastric Surgery**
M. R. WILLIAMS and J. M. PULLAN. *Lancet* [*Lancet*] **2**, 1013–1018, Nov. 14, 1953. 9 figs., 8 refs.

During the last 5 years 10 cases of severe diarrhoea, resulting in the death of 5 of the patients, have been seen at St. Thomas's Hospital, London, after the performance of partial gastrectomy, and similar cases have been reported from other sources.

The typical clinical picture was that on the 2nd or 3rd day after operation the patient developed epigastric colic, abdominal distension with active bowel sounds, and raised temperature, pulse, and respiration, followed by severe diarrhoea with circulatory collapse. If the condition was recognized and adequate fluid promptly given intravenously, immediate improvement occurred. In the 5 patients who recovered, the diarrhoea ceased in about a week and there were no permanent ill effects. At necropsy the changes observed were confined to the small intestine. In each case when the small bowel was opened it was found that the mucosa had sloughed, with separation of a membrane. In no case did the mucosal necrosis extend as high as the anastomosis, which appeared healthy in all cases. The submucosa was intact and isolated glands survived in the deeper parts of the mucosa. Cellular infiltration was slight, with a predominance of round cells and absence of polymorphs, there was no peritonitis, and the picture was not that of an acute infection. Examination of the stools revealed no organism common to all the cases. In 6 cases *Staphylococcus aureus* was obtained on culture, but the phage types were different and staphylococci of the same phage types were also found in other patients without diarrhoea. No special investigation for the presence of *Clostridium welchii* was made.

As to treatment, the authors recommend the early replacement of lost fluid by water, made isotonic with salt or glucose, until improvement occurs. Large volumes, up to 3 litres per hour, may be required in some cases, so that care must be taken not to overload the patient with sodium. Plasma or blood transfusion should be given in the initial phase to correct protein loss.

The authors are unable to suggest any explanation of causation. In most cases the operation had been uneventful, only a few of the patients had received sulphonamides or antibiotics before operation, though most of them had been given antibiotics after operation. Different surgeons performed the operations, and a variety of suture materials and operative techniques had been employed. *Norman C. Tanner*

Cardiovascular System

1325. **Gravitational Ulcer**
R. B. WRIGHT. *Lancet* [*Lancet*] **2**, 1273–1278, Dec. 19, 1953. 3 figs., 36 refs.

In this paper from the Western Infirmary, Glasgow, the author points out the difficulties of accurately assessing the pathological changes which occur in the veins of the lower limb, basing his experience on 284 consecutive cases of gravitational ulcer, in only 37 of which was there evidence of previous thrombosis of the deep veins. A positive response to Perthes's test has for many years been regarded as a proof of deep-vein thrombosis, but the fallacies of the test are clearly described. Venography is discussed and illustrated by reproductions of venograms, but the author [wisely] considers that this method of investigation is of little value so far as treatment is concerned; this also applies to venous blood pressure readings, the taking of which is time-consuming and the results misleading. The author concludes with a description of a scheme of treatment for the practical management of various types of leg ulcer.

[This is an instructive and critical review which should be studied by all surgeons who, from choice or necessity, are responsible for the treatment of the common and crippling condition of gravitational ulcer.]

R. J. McNeill Love

1326. **The Action of Procainamide on Auricular Arrhythmias.** (Action de la procaïne-amide sur les arythmies auriculaires)
N. BOYADJIAN and F. VAN DOOREN. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **46**, 941–948, Oct., 1953. 5 figs., 16 refs.

In experiments reported from the University of Brussels stable auricular fibrillation was produced in 20 dogs by Scherf's method. In all cases permanent reversion to normal rhythm followed the intravenous injection of procainamide in doses of 10 to 15 mg. per kg. body weight. Such doses caused no electrocardiographic abnormalities, but when 2 dogs were given 2·5 and 3 g. of procainamide respectively intravenously, prolongation of the P–R interval followed, with intraventricular block and ventricular extrasystoles, and one dog died from ventricular fibrillation.

In the treatment of auricular arrhythmias in man the drug had little effect by mouth. Given intravenously in doses of 0·3 to 0·5 g. it effectively, though briefly, suppressed auricular extrasystoles in 3 cases. In doses of 0·5 to 1·3 g. it corrected auricular paroxysmal tachycardia in 3 cases and auricular paroxysmal fibrillation of recent onset in 2. It was ineffective in established cases of auricular fibrillation.

When given intravenously procainamide may cause hypotension: it should therefore be given at a rate no greater than 0·1 g. per minute, the patient being recumbent and a watch being kept on his blood pressure. When given intramuscularly the drug does not lower the blood pressure, and having successfully corrected paroxysmal auricular fibrillation in 2 cases with intramuscular injections totalling 2 and 3 g. respectively, the authors consider that the administration of procainamide by this route merits further study. *J. A. Cosh*

CARDIOGRAPHY

1327. **The Electrocardiographic Pattern of Hypopotassemia with and without Hypocalcemia**
B. SURAWICZ and E. LEPESCHKIN. *Circulation* [*Circulation* (*N.Y.*)] **8**, 801–828, Dec., 1953. 12 figs., bibliography.

A detailed analysis is presented of the electrocardiographic findings in cases (culled from the literature, as well as from the authors' own experience) of hypopotassaemia with and without hypocalcaemia, both before and after the administration of potassium. Contrary to some previous reports, in pure hypopotassaemia no deviation from normal was found in the duration of any of the components of Q–U. The erroneous impression that the Q–T interval is prolonged in hypopotassaemia is attributed to the inclusion of the U wave and to the effect of other, co-existing, factors. In hypocalcaemia the Q–T interval is prolonged to a degree corresponding to the degree of prolongation of S–T, but the duration of Q–aU and of Q–U is unchanged. In combined hypopotassaemia and hypocalcaemia Q–T and its components are prolonged as in hypocalcaemia. Synchronous phonocardiography and electrocardiography show that mechanical systole is of normal or reduced duration in hypopotassaemia and is prolonged in hypocalcaemia. The " typical " electrocardiographic changes in hypopotassaemia are described as progressive depression of S–T, lowering and inversion of T, and an increase of U in left precordial leads. The differentiation of the hypopotassaemic pattern from the somewhat similar one sometimes obtained after the combined administration of digitalis and quinidine is discussed.

[The authors of this painstaking review have a tendency to be unable to see the wood for the trees. A little more coordination, with corresponding abbreviation, would have enhanced its value considerably.]

William A. R. Thomson

1328. **Further Studies in High Fidelity Electrocardiography: Myocardial Infarction**
P. H. LANGNER. *Circulation* [*Circulation* (*N.Y.*)] **8**, 905–913, Dec., 1953. 11 figs., 9 refs.

The technique of high-fidelity electrocardiography employs a cathode-ray oscillograph and an expanded time scale for the more detailed study of electrocardiographic patterns. In this report a comparison is made

of the records so obtained in 21 cases of healed myocardial infarction with those of 60 normal control subjects. In 14 of the former there was " a degree of high frequency detail which . . . was unquestionably in excess of that observed in any of [the] 60 normal controls ". Nine of these 14 patients had angina pectoris, compared with only one out of the remaining 7. It is suggested that this method may prove of value in the early recognition and prognosis of coronary disease.

[The introduction of high-fidelity electrocardiography opens up interesting prospects in the field of practical cardiology, though it is clear that much further work remains to be done in establishing norms.]

William A. R. Thomson

1329. **The Electrocardiogram in Congenital Heart Disease and Mitral Stenosis. A Correlation of Electrocardiographic Patterns with Right Ventricular Pressure, Flow, and Work**

R. S. Cosby, D. C. Levinson, S. P. Dimitroff, R. W. Oblath, L. M. Herman, and G. C. Griffith. *American Heart Journal* [*Amer. Heart J.*] **46**, 670–682, Nov., 1953. 4 figs., 15 refs.

At the Los Angeles County Hospital (University of Southern California) the electrocardiographic pattern was correlated with right ventricular pressure, flow, and work in (1) 55 patients with mitral stenosis and (2) 64 with congenital heart disease, in all of whom the right ventricular pressure was greater than 30 mm. Hg. In only 28 (51%) of the cases in Group 1 was the electrocardiogram (ECG) abnormal, compared with 61 (91%) of those in Group 2. Of the abnormal records, 19 in Group 1 and 31 in Group 2 showed the pattern of right ventricular hypertrophy, while 9 in Group 1 and 28 in Group 2 showed that of partial right bundle-branch block.

There were clear-cut differences between the electrocardiographic patterns of right ventricular hypertrophy as seen in the two groups. The mean height of RV_{3R} in Group-2 cases was almost 3 times greater than in those in Group 1, RV_1 in Group 2 was almost twice as high as in Group 1, the R:S ratio in V_{3R} was approximately 3 times as great, and the pre-intrinsicoid deflection time in V_1 was longer. Similar differences were found on comparing the signs of partial right bundle-branch block in the two groups; in both V_1 and V_{3R} the mean height of R in Group-2 cases was approximately 3 times as great as in Group-1 cases.

In Group 1 the ECG was often normal (or borderline) in the presence of mean right ventricular systolic ejection pressures up to 60 mm. Hg, but in Group 2 the ECG was abnormal in all cases in which the mean pressure level was above 30 mm. Hg. Similarly, whereas in Group 1 the ECG was often normal when the right ventricular work load was more than 1 kg. m. per min. per sq. m., above this level the ECG in Group-2 cases was practically always abnormal.

In both groups the pattern of partial right bundle-branch block was found at almost all levels of right ventricular pressure and work, and the authors therefore conclude that " this pattern appeared to be almost as significant as the classic pattern of right ventricular hypertrophy in the detection of right ventricular hypertension and presumptive right ventricular hypertrophy ". The differences in the total electrocardiographic picture are taken to indicate fundamental differences in the genesis of right ventricular hypertrophy in the two conditions.

William A. R. Thomson

CONGENITAL HEART DISEASE

1330. **The Electrocardiogram in Patent Ductus Arteriosus. A Study of 52 Cases Treated by Operation.** (L'électrocardiogramme dans la persistance du canal artériel. Étude de 52 cas personnels opérés)

G. Dauzier, M. Durand, and C. Metianu. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **46**, 994–1007, Nov., 1953. 5 figs., 28 refs.

In this communication from the Hôpital Broussais, Paris, the authors report the results of an electrocardiographic study of 52 patients before operation for repair of a patent ductus arteriosus and in 28 of these after ligation of the ductus; 37 (70%) of the patients were under 15 years of age, and only 3 were over 30. At least 12 routine leads were taken for each patient.

In 14 cases the electrocardiogram was found to be normal. In 29 cases it showed the presence of left ventricular hypertrophy, either isolated (23 cases), or associated with right or left bundle-branch block (6 cases), and associated with auricular hypertrophy in 4 cases. Combined ventricular hypertrophy was demonstrated in 7 cases, in 2 of which there was also incomplete right bundle-branch block. Finally there were 2 electrocardiograms showing isolated, incomplete, right bundle-branch block. The authors attempt to correlate these electrocardiographic findings with the radiological appearances and the condition as revealed at operation; they also describe the changes in the cardiographic patterns following ligation of the ductus arteriosus.

[For fuller details the original paper should be consulted.]

A. I. Suchett-Kaye

1331. **Problems in the Diagnosis and Surgical Treatment of Pulmonic Stenosis with Intact Ventricular Septum**

J. W. Kirklin, D. C. Connolly, F. H. Ellis, H. B. Burchell, J. E. Edwards, and E. H. Wood. *Circulation* [*Circulation* (*N.Y.*)] **8**, 849–863, Dec., 1953. 13 figs., 44 refs.

The authors discuss the pathological anatomy of the pulmonary outflow tract in cases of pulmonary stenosis without interventricular septal defect and describe the results of operation in 12 cases at the Mayo Clinic. It is pointed out that obstruction to the pulmonary blood flow may occur at the valve, in the infundibulum, or at both sites. Pure infundibular stenosis was not found in the 6 cases in the series which came to necropsy. There was marked hypertrophy of the muscle of the right ventricle which, in 4 of the 6 hearts examined, was sufficient to cause significant narrowing of the outflow tract.

The authors discuss the identification of the type of stenosis by preoperative catheterization, by inspection and palpation of the right ventricular outflow tract at

operation, and by catheterization via the right ventricle under direct vision during operation. They emphasize that exact anatomical identification is essential for the proper surgical management of the stenosis, and that continuous pressure recordings made by direct catheterization during the operation are of value in ensuring that adequate dilatation of the valvular orifice has been carried out.

It was found that although the right ventricular pressure fell sharply after dilatation, it might not reach a normal level for some months. The pressure fell most markedly in cases of pure valvular stenosis, but also fell considerably where a combined stenosis was encountered. It is suggested that a continued fall in pressure after valvotomy in the presence of infundibular stenosis may well be due to diminution in the hypertrophy of the right ventricular muscle, which is, at least in part, responsible for the infundibular stenosis.

The authors operate on asymptomatic patients only when the right ventricular pressure exceeds 75 mm. Hg. Of the 12 patients, 2 died as a result of the operation.

[This is an excellent paper, well worth reading in the original.] *J. R. Belcher*

1332. **Persistence of Left Superior Vena Cava**
I. STEINBERG, W. DUBILIER, and D. S. LUKAS. *Diseases of the Chest* [*Dis. Chest*] **24**, 479–488, Nov., 1953. 6 figs., 18 refs.

Eleven cases of persistent left superior vena cava discovered during life by cardiac catheterization and angiocardiography are described and illustrated. By itself, a persistent left superior vena cava produces no detectable effects on the function of the heart but it is often associated with other congenital cardiac anomalies often of a multiple complex type.—[Authors' summary.]

PERICARDIUM

1333. **Mechanical and Myocardial Factors in Chronic Constrictive Pericarditis**
R. M. HARVEY, M. I. FERRER, R. T. CATHCART, D. W. RICHARDS, and A. COURNAND. *Circulation* [*Circulation (N.Y.)*] **8**, 695–707, Nov., 1953. 11 figs., 12 refs.

Detailed studies, including cardiac catheterization, carried out at Bellevue Hospital (Columbia University), New York, on 5 patients with constrictive pericarditis showed there to be important variations from the uniform clinical and physiological picture usually accepted as characteristic of this disease, in which the mechanical effects of an inelastic pericardium are considered to be the salient factor. Although the mechanical factor was in fact the dominant one in the first case, closer study of the pressures suggested that the distensibility characteristic of the pericardium replaced that of the individual chambers; the larger difference between oncotic pressure on the one hand and capillary hydrostatic pressure in the lesser and systemic circulations on the other may explain why frank pulmonary oedema is rare in patients with constrictive pericarditis even in the presence of considerable systemic congestion. It is suggested that the characteristic post-systolic and early diastolic dip in the ventricular and auricular pressure tracings is due to the forces of the inelastic pericardium which become operative suddenly at the end of systole. In the second case it was demonstrated that the haemodynamic abnormalities associated with constrictive pericarditis (elevation of right ventricular diastolic pressure, early right ventricular diastolic dip, fall of cardiac output after administration of digoxin) may exist in the absence of any clinical signs of congestion, and in the third an extensively calcified pericardium was found unaccompanied by signs of congestion. In the fourth case, in which the haemodynamic findings were mostly typical of constrictive pericarditis, the favourable results obtained with digoxin emphasized the importance of myocardial failure in this disease; the role played by an inelastic pericardium was not fully elucidated in this case. In the fifth case many of the signs of congestion were found to be reversible under treatment with rest, digitalis, and diuretics.

The conclusion is drawn from the study of these cases that generalized hypervolaemia and myocardial insufficiency may contribute to the clinical picture of constrictive pericarditis in addition to the mechanical restriction imposed by an inelastic pericardium, that they may be important factors in some cases, and that in consequence each case requires detailed study.
A. Schott

1334. **Acute Idiopathic Pericarditis**
E. M. GOYETTE. *Annals of Internal Medicine* [*Ann. intern. Med.*] **39**, 1032–1044, Nov., 1953. 9 figs., 12 refs.

The author describes 28 cases of acute idiopathic pericarditis seen at Fitzsimons Army Hospital, Denver, Colorado, during a recent 3½-year period. The ages of the patients ranged from 18 to 63, but only 4 were over 50. In 17 cases there was a history of a preceding upper respiratory infection. The onset was abrupt in 19, less acute in 8, and insidious in one. Pain, which was the presenting symptom in all cases, was localized in the mid-chest in 17, occurring in all parts of the left chest in the remainder. It was intermittent in character and often intensified by respiration. A pericardial rub was heard in the 23 cases seen at an early stage of the illness; this persisted for days or months, and in some cases disappeared only to return a few days later. Radiological examination showed enlargement of the heart shadow in 6 cases, there being considerable pericardial effusion in 2. An associated pleural effusion was noted in 2 cases. Pericardial fluid, which was examined in 4 cases, contained many cells, 80 to 95% of which were lymphocytes. Pericardial biopsy in one case showed non-specific inflammatory changes. Characteristic changes were observed in the electrocardiogram (ECG) in all but one case.

The illness lasted from a few days to 4 months, averaging 3 to 4 weeks. One patient had two attacks. The author draws attention to the importance of the differential diagnosis from myocardial infarction, which was originally diagnosed in 22 of the 28 cases. The main distinguishing features of pericarditis are the absence of

shock, the occurrence of a pericardial rub, fever, and leucocytosis at the onset of the pain, accompanied by changes in the ECG. Antibiotic therapy was without any effect on the course of the disease in the cases described.

C. Bruce Perry

CORONARY DISEASE AND MYOCARDIAL INFARCTION

1335. Penta-erythritol Tetranitrate in Treatment of Angina

D. WEITZMAN. *British Medical Journal* [*Brit. med. J.*] **2**, 1409–1412, Dec. 26, 1953. 1 fig., 11 refs.

In a well-controlled study carried out at the National Heart Hospital, London, penta-erythritol tetranitrate (PETN), a long-acting vasodilator, was given in 60-mg. doses 3 times daily to 34 of 65 patients with angina pectoris, the other patients receiving dummy tablets of identical appearance. The drug had no effect on blood pressure, but side-effects were observed in 8 cases—lethargy, digestive upset, headache, and visual disturbance; in 3 of these patients the treatment had to be stopped. No long-term toxic effects or diminished effectiveness were noted in the other patients after 6 to 12 months of treatment. Electrocardiographic studies showed that oral administration of 120 mg. of PETN could abolish the depression of the ST segment induced by exercise, this effect being obtained within 15 minutes and lasting for 4 hours.

The results of treatment were analysed in terms of increase in effort tolerance, decrease in the severity of the pain brought on by effort, and reduction in requirement of supplementary glyceryl trinitrate. Of the 34 patients receiving the drug, 8 showed increased effort tolerance, and 6 had less severe angina or required less glyceryl trinitrate; of the 31 control patients, 3 patients in each of these two categories showed similar improvement. When PETN was substituted for dummy tablets in 15 of the control cases, one patient showed improved exercise tolerance and 2 had less severe angina. Out of 15 patients deriving benefit from PETN, complete withdrawal of the drug in 7 cases caused a return of symptoms to their previous severity in 5; but of the remaining 8 patients, who were given dummy tablets in replacement, 5 showed no clinical deterioration.

The author considers that penta-erythritol tetranitrate has some value in preventing disturbed sleep from nocturnal angina, and that it may be usefully given in addition to glyceryl trinitrate in a selected minority of patients.

K. G. Lowe

1336. Resection of Anginal Pathway for Relief of Anginal Pain

J. A. EVANS and J. L. POPPEN. *New England Journal of Medicine* [*New Engl. J. Med.*] **249**, 791–796, Nov. 12, 1953. 3 figs., 14 refs.

In patients undergoing extended sympathectomy for arterial hypertension at the Lahey Clinic, Boston, concomitant angina pectoris was frequently found to be relieved if the resection of the sympathetic chains was extended to include the 4th thoracic ganglia. For the relief of hypertensive patients with mild anginal pain, resection to below this level is considered sufficient; for more severe angina, sympathectomy including bilateral removal of the 1st to 4th thoracic ganglia (the "anginal pathway") is thought desirable. In the technique employed by the authors, portions of the 8th and 11th ribs are removed to permit of excision of the lower thoracic chain in operations for arterial hypertension; to reach the upper part of the chain a portion of the 5th rib is resected in addition. In normotensive patients requiring only upper thoracic sympathectomy, a portion of the 4th rib alone is removed.

The results in 16 patients with angina pectoris are reported. In all but one of these the angina was disabling, and 14 of them also had hypertension. The extent of the resection varied; on the left side the 1st ganglion was usually included, but on the right the 1st to the 3rd ganglia were less often excised. Relief of anginal pain was complete in 5 cases and satisfactory in 8; that is, 13 of the 16 patients benefited. Severe postural hypotension which followed this extensive sympathectomy in hypertensive patients did not induce angina except in one patient. Dilatation of the coronary arteries as a result of sympathectomy is suggested as a possible reason for this. [Severance of the pain pathways might equally be responsible.] The suggestion is also made that the mechanism of status anginosus may be that of a reflex sympathetic dystrophy: this would add further reason for operating on such cases. [In the abstracter's view the reasoning is, however, unconvincing.]

C. J. Longland

1337. L-Noradrenaline in Treatment of Shock in Cardiac Infarction

K. SHIRLEY SMITH and A. GUZ. *British Medical Journal* [*Brit. med. J.*] **2**, 1341–1345, Dec. 19, 1953. 3 figs., 12 refs.

The prolongation of the severe shock which usually accompanies cardiac infarction gravely influences the prognosis. The authors briefly review previous methods of treating such cases, and in view of the claim made by anaesthetists that the laevo-rotatory form of noradrenaline obviates serious falls of blood pressure during major operations, decided to try this substance in cardiogenic shock.

In 6 such cases, treated at Charing Cross Hospital, London, the method was used when the systolic blood pressure was progressively falling or had remained below 80 mm. Hg for 24 hours, especially if there was also oliguria or a very low pulse-pressure; 2 of the patients were pulseless when the infusion was begun. To a litre of 5% dextrose solution or of 4·3% dextrose in 0·18% saline (not normal saline, to avoid excess of sodium ions), 4 ml. of a 1-in-1,000 L-noradrenaline bitartrate solution was added, giving a concentration of the drug of 4 μg. per ml. This was given as an intravenous drip infusion, the rate being adjusted as indicated by frequent readings of the blood pressure, the aim being to keep the systolic pressure between 100 and 110 mm. Hg. Where it was necessary to give large doses the concentration of

L-noradrenaline was increased in order to maintain a reasonably slow rate of infusion; in one case the concentration was raised to 64 ml. per litre. Details are given of the 6 cases. The infusion was maintained over periods varying from 3 hours to 8 days; the process of discontinuation of the infusion had in some cases to be very gradual to avoid a dangerous fall in systolic pressure. Clinical improvement was immediately apparent in each case, with rise of systolic pressure and recovery of consciousness when this had been lost. Of the 6 patients, 2 who were shown at necropsy to have recent as well as old infarctions died within 4 days, but 4 recovered, although one of these died of congestive heart failure 4 months later; the other 3 patients were still well 6 to 13 months later.

The authors discuss the mode of action of the drug and the indications for its use, and compare their results with those reported in other cases treated similarly.

R. S. Stevens

1338. **Subendocardial Ischaemia of the Left Ventricle and Coronary Insufficiency.** (Ischémie sous-endocardique ventriculaire gauche et insuffisance coronarienne)

P. CHICHE, J. BAILLET, and R. VERDUN DI CANTOGNO. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **46**, 865–897, Oct., 1953. 16 figs., bibliography.

This lengthy review of the morbid anatomy, aetiology, and electrocardiography of subendocardial ischaemia is based on a study of 42 cases at the Hôpital Lariboisière, Paris.

The hearts examined post mortem were usually hypertrophied; sometimes ecchymoses were visible on the subendocardial surface, particularly when death had occurred suddenly. On section the most characteristic macroscopic feature of the condition was the distribution of the lesions in the innermost layer of the myocardium, forming a sharp contrast with the apparently normal surrounding muscle. The left ventricle was usually affected rather than the right, with lesions roughly encircling the middle of the ventricle and often more marked on the antero-lateral and septal walls. The cut surface might show pallor, or patches of vascular injection with ecchymoses, or fine pink mottling against a pale or scarred background. Frank necrosis was uncommon. Microscopically, there was a mixture of the types of cellular change which may follow ischaemia—muscle-cell degeneration, interstitial oedema, and infiltration with polymorphonuclear leucocytes and monocytes—intermingled with which might be scar tissue or occasional patches of normal muscle. The authors stress the difference between the limited and clear-cut appearance of infarction following obstruction of a single artery and the widespread and variable pattern of subendocardial ischaemic lesions. They consider the latter to be due to a generalized insufficiency in the coronary flow, which may be due to the joint effect of a variety of causes, both organic and functional.

Of the 42 cases studied, 12 were due to coronary atheroma and 6 to frank coronary thrombosis, 7 were syphilitic, in 6 there was aortic valvular stenosis, and 9 were associated with extracardiac causes (pulmonary embolism in 6, shock in 2, and haemorrhage in 1). The electrocardiogram generally showed the pattern of left ventricular strain.

Possible causes for the selective involvement of the deeper layers of the myocardium are discussed, and contributory causes, both organic and functional, are considered in detail.

J. A. Cosh

1339. **Tobacco and the Coronary Arteries.** (Tabac et coronaires)

H. FABRE and Y. LINQUETTE. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **46**, 898–904, Oct., 1953. 3 figs., 26 refs.

In experiments carried out at the Faculty of Medicine of Bordeaux, the authors studied the effect of the inhalation of tobacco smoke upon the electrocardiogram (ECG) of 19 normal dogs and 10 in which the first major left-sided branch of the anterior descending coronary artery had been ligated. In each animal an endotracheal tube was inserted under general anaesthesia, and the tube was connected intermittently with a cigarette holder until the animal had inhaled the smoke from one or two *gauloises bleues*. The ECG was recorded before, during, and after each inhalation, continuing until any abnormalities had disappeared.

Of the 19 intact dogs, the ECG of 6 showed no change, but in 4 cases there was displacement of the S–T segment and in 12 there were changes in the T wave. Of the 10 dogs with coronary ligation, the ECG of 3 was unaffected, while displacement of S–T was present in 3 and T-wave changes in 6. Such changes usually disappeared within 4 minutes of ceasing the inhalation of smoke. There was thus no significant difference in the effect of tobacco smoke between the two groups.

J. A. Cosh

HEART FAILURE

1340. **The Diuretic Action of Potassium Associated with a Low-sodium Diet in the Treatment of Cardiac Oedema (Preliminary Report).** (L'azione diuretica del potassio associata a dieta povera di sodio nel trattamento degli edemi cardiaci (Primi risultati))

G. MEZZASALMA and C. BRENTANO. *Ospedale maggiore* [*Osped. maggiore*] **41**, 353–368, Aug., 1953. 10 figs., bibliography.

The authors, having observed that the sodium content of oedema fluid is high and its potassium content low, deduce from this that in cases of congestive heart failure there is a potassium–sodium imbalance. They suggest that in such patients the intracellular level of potassium is low, and that oral administration of potassium salts restores this level to normal, with resulting mobilization of sodium and excretion of oedema fluid.

They have tested this hypothesis at the Maggiore Hospital, Milan, in 10 selected cases of congestive heart failure in which routine therapy had proved ineffective, giving a mixture of potassium salts by mouth. This mixture consisted of potassium citrate (50%), succinate (20%), maleate (20%), and tartrate (10%), and contained

38% of potassium. The patients were given 4 to 10 g. daily, divided into 4 doses, and all were placed on a low-salt diet (estimated sodium chloride content 2 g. daily) with a restricted fluid intake. In each case diuresis occurred and there was a fall in weight as the oedema resolved; the diuresis was maintained for some days after cessation of administration of potassium. No toxic effects were observed and no deleterious change took place in the electrocardiogram of any of the patients.

D. Weitzman

1341. **Ligation of the Inferior Vena Cava in 26 Cases of Heart Failure.** (Remarques à propos de 26 ligatures de la veine cave inférieure dans l'insuffisance cardiaque)
H. WELTI, C. LIAN, and J. DAZZI. *Mémoires de l'Académie de chirurgie* [*Mém. Acad. Chir. (Paris)*] **79**, 624–628, Oct. 14, 1953.

The immediate effects of ligation of the inferior vena cava for the relief of cardiac insufficiency are good, dyspnoea and liver enlargement being diminished although the effect on oedema of the legs is variable. Ligation is especially indicated in mitral regurgitation, but is contraindicated in cases of long-standing heart failure or failure due to arterio-venous fistula.

The late results, however, are poor. Out of 26 cases treated by the authors at the Hôpital de la Pitié, Paris, 17 of the patients died within 18 months. Of the other 9 patients, 7 have survived for more than 6 months, and the results in 3 of these were classed as " very good " and in one as " good ", while 3 relapsed after good initial improvement. Complications have included venous thrombosis in 4 cases. The authors perform the operation extraperitoneally, with local and light general anaesthesia. Their operative mortality (one death) was low, in contrast to figures reported by other workers. The patient who died had a femoral arterio-venous fistula and the vena cava was considerably dilated.

S. F. Stephenson

1342. **Antibiotic Prophylaxis in Chronic Congestive Failure**
L. V. MCVAY, D. H. SPRUNT, and T. N. STERN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **226**, 491–503, Nov., 1953. 1 fig., 31 refs.

In an attempt to reduce the incidence of respiratory infection in cases of chronic congestive heart failure the authors tried prolonged administration of aureomycin in 73 cases at the John Gaston Hospital (University of Tennessee). A dose of 250 mg. of aureomycin was given one hour before breakfast and repeated 2 hours after supper each day. A control group of 76 patients with chronic congestive heart failure received a placebo. The patients were observed for 1½ to 2 years; during that time 9 of the treated patients and 15 of the controls died. A " definite reduction " in the incidence of respiratory infection was observed in the treated group compared with the controls. One of the treated patients and 4 of the controls developed bronchopneumonia. The erythrocyte sedimentation rate tended to be lower and the haematocrit value to be higher in the treated group than in the controls, while liver function, which was abnormal in both groups before the test, tended to become normal more frequently in the patients receiving aureomycin. There were no severe side-reactions to the drug; diarrhoea in 6 and pruritus ani in 4 of the treated group responded to simple symptomatic treatment. Nausea and vomiting were equally common in both groups. A sense of well-being was noted by rather more of the treated patients than of the controls.

Bone-marrow biopsy did not reveal any abnormality in either group. The faecal flora in both groups were comparable, except for the presence of aureomycin-resistant strains of *Streptococcus faecalis* in faecal specimens from treated patients. There was no evidence of overgrowth of *Pseudomonas aeruginosa*, *Staphylococcus aureus*, or *Candida albicans* in the 13 treated cases which came to necropsy.

D. W. Barritt

CHRONIC VALVULAR DISEASE

1343. **Tricuspid Insufficiency. Observations Based on Angiocardiography and Cardiac Catheterization in Twelve Patients**
C. T. DOTTER, D. S. LUKAS, and I. STEINBERG. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **70**, 786–792, Nov., 1953. 6 figs., 9 refs.

Angiocardiography and cardiac catheterization were carried out in 12 cases of tricuspid insufficiency at the New York Hospital–Cornell Medical Center, and in this paper the findings are discussed. All the patients had chronic rheumatic mitral stenosis and auricular fibrillation.

It is pointed out that in some cases of tricuspid insufficiency there are typical clinical features (these are briefly indicated); of the present series the condition was diagnosed from clinical findings in 6 cases. Angiocardiography reveals dilatation of the right atrium and superior vena cava and, occasionally, a filling defect in the right atrium which is not constant in shape and is the result of regurgitation of right ventricular blood through the incompetent tricuspid valve. Cardiac catheterization is the most accurate diagnostic method, the diagnosis being established by this means in all 12 cases. A significant feature of the pressure curve was a high plateau in tracings from the right atrium.

The authors do not consider that the presence of tricuspid insufficiency contraindicates operation on the mitral valve.

Sydney J. Hinds

1344. **Respiratory and Circulatory Studies of Patients with Mitral Stenosis**
P. C. CURTI, G. COHEN, B. CASTLEMAN, J. G. SCANNELL, A. L. FRIEDLICH, and G. S. MYERS. *Circulation* [*Circulation (N.Y.)*] **8**, 893–904, Dec., 1953. 3 figs., 28 refs.

At the Massachusetts General Hospital, Boston, 16 patients with mitral stenosis were investigated before operation by means of cardiac catheterization and ventilatory and respiratory tests. The patients deemed to have the most severe mitral stenosis were found to have the highest pulmonary arterial resistance and the lowest resting cardiac output. Most of the patients

showed a reduced vital capacity and a decreased maximum breathing capacity. The oxygen diffusing capacity was reduced in proportion to the severity of the disease and this finding was corroborated by lung biopsy, which showed thickening and fibrosis of the alveolar walls, a condition likely to hinder adequate oxygen diffusion. The degree of the pulmonary arterial and arteriolar changes found in lung-biopsy specimens, however, was not correlated with the calculated pulmonary arteriolar resistances.

Of 4 cases seen 6 months after operation, 3 showed a reduction of pulmonary arterial pressure, and in all 4 there was a decrease in pulmonary arteriolar resistance. This diminution in pulmonary arteriolar resistance, which was not correlated (even before operation) with any pathological change in the smaller blood vessels of the lung, is remarkable and, in the authors' view, suggests that a reversible vasoconstriction may play the determining part in the pathogenesis of pulmonary hypertension in mitral stenosis. *James W. Brown*

1345. **Relief of Pulmonary Hypertensive Pain after Mitral Commissurotomy**

E. J. MEARS, W. P. HARVEY, and C. A. HUFNAGEL. *New England Journal of Medicine* [*New Engl. J. Med.*] **249**, 715–718, Oct. 29, 1953. 6 figs., 3 refs.

A case of a woman with mitral stenosis who was incapacitated because of precordial pain simulating that of coronary disease and present daily for at least 15 years is reported. Morphine and " demerol " [pethidine] had been required to such an extent for relief that some observers thought that the patient was an addict.

After successful operation on the mitral valve there was an immediate and dramatic relief of pain, and follow-up examination after 5 months revealed that the patient was free of this pain, which had incapacitated her before operation. She appears to be proof of the validity of pulmonary hypertensive pain as an entity, and this case offers strong evidence that the etiology of the pain is related to increased pressure in the pulmonary circuit.—[Authors' summary.]

1346. **Commissurotomy for Aortic Stenosis**

C. P. BAILEY, H. E. BOLTON, W. L. JAMISON, and H. B. LARZELERE. *Journal of the International College of Surgeons* [*J. int. Coll. Surg.*] **20**, 393–408, Oct., 1953. 10 figs., 7 refs.

After the mitral valve, the aortic valve is the most common site of rheumatic involvement. Stenosis of the aortic valve occurs as a result of fusion between the valve edges, which begins at the aortic wall and may continue until only a small, irregular, central opening is left. The method developed by the authors at the Hahnemann Hospital, Philadelphia, for the surgical relief of the stenosis by direct and forcible dilatation has been described elsewhere (Larzelere and Bailey, *J. thorac. Surg.*, 1953, **26**, 31; *Abstracts of World Medicine*, 1954, **15**, 141). By means of a transventricular approach, a guide is passed through the stenosed orifice and a special dilator is then passed over the guide and led into the opening. This specially designed instrument works on the principle of a Kollman's urethral dilator, but its blade unit is free to rotate so that the 3 blades will engage in the commissures between the fused cusps and split them when the dilator is expanded.

The authors now record the use of this method in 77 cases of aortic stenosis, in more than half of which there were coexistent mitral lesions. The operation mortality was 15·6%, with an unexpectedly high proportion of fatalities among the patients with isolated aortic lesions (7 out of 35, compared with 5 deaths among 42 patients with combined lesions). In 7 cases aortic insufficiency resulted from, or was increased by, the operation.

In spite of these excellent pioneer results the authors are dissatisfied with the method and are critical of the transventricular approach because of technical difficulties and the possibility of damage to the soft left ventricular muscle. A retrograde approach has therefore been developed which permits palpation of the valve from above and allows the finger to be used in directing instruments through the stenosis. The technique described consists in exposing the ascending aorta through a trans-sternal incision and cutting free a large square of pericardium. This is stitched to the aorta about 1½ inches (38 mm.) above the valve and its free ends caught in a purse-string suture which allows the pericardium to be pouched round the finger. A piece of aorta is then pinched up with a curved Potts clamp so as to allow an incision to be made into its lumen through the sutured pericardium. The finger and the dilator are then introduced simultaneously, blood loss being prevented by pulling the purse-string tight, and dilatation carried out under direct palpation. At the completion of this procedure the aorta is again clamped and the incision closed. Further modifications are being made in this technique, which has been carried out on 11 occasions with 3 deaths. The retrograde method is probably the operation of choice in cases of isolated or pure aortic stenosis, but where mitral valvotomy has also to be undertaken the left transventricular approach to the aortic valve is more suitable. *T. Holmes Sellors*

1347. **Reactivation of Rheumatic Fever following Mitral Commissurotomy**

L. A. SOLOFF, J. ZATUCHNI, O. H. JANTON, T. J. E. O'NEILL, and R. P. GLOVER. *Circulation* [*Circulation (N.Y.)*] **8**, 481–493, Oct., 1953. 10 figs., 8 refs.

The authors draw attention to a syndrome that they have noted as a sequel to mitral valvotomy. The symptoms, mainly precordial pain and fever, have been noted in 43 out of 179 cases of mitral stenosis treated by commissurotomy (24%) and are regarded as something separate from the ordinary complications that may arise in the course of any thoracic operation. In 24 additional cases the patient complained of pain, coming on after discharge from hospital, which was of a similar nature but unaccompanied by fever.

The onset of pain is sudden and may take place anything from 10 days to a month after operation. It is gripping and vice-like over the pericardium, radiates over a wide field, may last several weeks, and may recur.

Associated with the pain is a variable degree of fever, which is accompanied by toxaemia, weakness, and sweating. Other features, such as psychosis, heart failure, and arthritis, may be added to the picture, the cardiac symptoms being the most important. The most likely explanation is that there has been a reactivation of the rheumatic process; the 179 cases included in this study formed part of a consecutive series of 183, 4 having been excluded because the operation was followed immediately by acute rheumatic fever. Biopsy of the left atrial appendage was taken at operation in 37 of the 43 cases in which the syndrome subsequently developed. Aschoff bodies were identified microscopically in 15 (40·5%) of these, but also in a practically identical percentage of cases in which the syndrome did not occur.

The fate of the 43 patients who developed the syndrome was varied—3 died, 2 developed hemiplegia, 3 became psychotic, and 5 went into permanent auricular fibrillation. Of the remaining 30, the majority require as much medical attention as they did before the operation, or more.

The authors do not discuss the implication of these findings for the selection of patients for operation beyond insisting on the desirability of excluding patients with clinically active rheumatism and commenting on the difficulty of recognizing this condition.

T. Holmes Sellors

HYPERTENSION

1348. **Urethral Apoplexy: an Early Symptom of Malignant Hypertension**

S. C. Pascoe and J. M. Evans. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **226**, 533–536, Nov., 1953.

Four patients with hypertension in the malignant phase have been presented. In each instance spontaneous urethral bleeding was either the initial symptom or appeared early in the disease. The infrequency of the reported occurrence of urethral hemorrhage associated with malignant hypertension has been emphasized. The occurrence of bladder and urethral hemorrhages in experimental hypertension and experimental renal insufficiency is noted and its possible relation to human findings is discussed.—[Authors' summary.]

1349. **Studies on the Control of Hypertension by Hyphex. II. Toxic Reactions and Side Effects**

J. D. Morrow, H. A. Schroeder, and H. M. Perry. *Circulation* [*Circulation (N.Y.)*] **8**, 829–839, Dec., 1953. 1 fig., 6 refs.

" Hyphex ", a combination of hydrallazine and hexamethonium, has been used by the authors at Barnes Hospital, St. Louis, in the treatment of 258 patients with hypertension for periods of 6 to 25 months. In a previous paper (*Circulation*, 1953, **8**, 672; *Abstracts of World Medicine*, 1954, **15**, 317) the clinical results were reported; in the present paper the toxic effects of these drugs are considered.

In most cases one or the other of the constituent drugs produced some side-reaction. In cases in which there was organic partial obstruction in a hollow viscus, complete obstruction was liable to develop causing, for example, retention of urine if there was prostatic hypertrophy, or complete intestinal obstruction in the presence of old adhesions. Hexamethonium was particularly incriminated for these effects. Hydrallazine alone was shown to increase anginal pain in some cases, but hyphex completely relieved anginal pain in 7 cases. Hydrallazine also tended to cause pyrexia, and in 16 cases after prolonged treatment there developed a syndrome indistinguishable from rheumatoid arthritis, and if treatment was persisted with, a collagen-disease-like condition closely resembling disseminated lupus erythematosus. Fatal interstitial pneumonia occurred in 5 cases treated with hyphex.

The authors feel that in spite of these adverse reactions and side-effects the use of hyphex is a valuable and practical method of treating hypertension, provided that precautions are taken to minimize serious consequences, since in most cases the benefits obtained outweighed the risks; neither agent, however, is ideal.

James W. Brown

1350. **Newer Drugs in the Treatment of Hypertension. I. Use of Hexamethonium Salts**

H. A. Sieber, K. S. Grimson, and E. S. Orgain. *Circulation* [*Circulation (N.Y.)*] **8**, 840–848, Dec., 1953. 20 refs.

Fifty patients exhibiting relatively severe, stable or progressive hypertension were treated with hexamethonium compounds over periods of 3 to 19 months for an average of 9 months per patient. Good control of blood pressure by hexamethonium as evidenced by average recumbent blood pressure levels of 160/110 or less was recorded for three treatment periods as follows: (1) during hospitalization, 16 patients (40%); (2) during first four months of outpatient care, 8 patients (16%); (3) during the subsequent 5 to 19 months, 3 patients (6%). Postural changes in blood pressure were uniformly greater.

Hexamethonium is a potent anticholinergic agent capable of lowering blood pressure for short periods. During prolonged administration the initial effects upon blood pressure tend to become diminished or lost, so that in the long-term treatment of severe hypertension, hexamethonium therapy alone possesses limited value.

Frequent amelioration of hypertensive symptoms and occasional decrease in retinopathy and improvement in the electrocardiogram are noted. Heart size and renal function have not been altered significantly.

Five deaths occurred during the treatment period, but in no instance was the fatality attributed directly to drug action. In addition many serious complications were observed, but these, with one exception, appear to reflect the severity of the hypertensive disease rather than a deleterious effect of the drug itself.—[Authors' summary.]

1351. **Toxic Effects of 1-Hydrazinophthalazine in Ambulatory Hypertensive Patients**

M. H. Wald, M. I. Fierro, and K. H. Keeton. *American Heart Journal* [*Amer. Heart J.*] **46**, 861-864, Dec., 1953. 1 fig., 10 refs.

Haematology

ANAEMIA

1352. **Chronic Familial Nonspherocytic Hemolytic Anemia**
E. L. LIPTON, H. J. GROSSMAN, and J. B. RICHMOND. *Pediatrics* [*Pediatrics*] **12**, 384–394, Oct., 1953. 6 figs., 35 refs.

A new type of haemolytic anaemia occurring in two sisters is reported from the University of Illinois College of Medicine, Chicago. The patients, who became anaemic shortly after birth, and a healthy brother were born to normal parents of European descent with no definite family history of anaemia. Radiographs of the affected sisters showed prominent trabeculae and punched-out areas in the cancellous bones; the cortex was thinned and the diploë of the skull thickened. The osmotic fragility of the erythrocytes was normal and the lysolecithin fragility diminished. The older and more severely affected sister had slight icterus, splenohepatomegaly, enlargement of the heart, generalized enlargement of the lymph nodes, and an infection of the upper respiratory tract when first seen by the authors at the age of 23 months. The marrow showed normoblastic hyperplasia and the faecal urobilinogen content was increased, but there was no reticulocytosis. From the age of 3 months until splenectomy was performed at $5\frac{1}{2}$ years she received more than 70 transfusions, but has since received none. The younger sister underwent splenectomy at the age of $4\frac{3}{4}$ years, with marked symptomatic improvement. The condition appeared to be a congenital haemolytic anaemia not due to any of the known abnormalities of the erythrocyte.

George Discombe

1353. **Sickle-cell Anemia Crisis. Report on Seven Patients Treated with Priscoline**
E. SMITH, P. ROSENBLATT, and A. V. BEDO. *Journal of Pediatrics* [*J. Pediat.*] **43**, 655–660, Dec., 1953. 15 refs.

During treatment of pain of vasospastic origin in poliomyelitis with benzazoline (" priscoline ") a striking similarity was observed to the pain of the sickle-cell anaemia crisis. Benzazoline was therefore tried in 7 cases of sickle-cell anaemia at Kings County Hospital, Brooklyn, New York.

The patients, all negro children, were admitted to hospital acutely ill with symptoms suggestive of various other diseases, the diagnosis of sickle-cell anaemia being established only after admission. A prominent feature in all cases was pain in the viscera or limbs, which was relieved by administration of benzazoline. The authors submit that their findings support the theory that vascular spasm is an important feature of the crisis of sickle-cell anaemia. They also suggest [with rather less reason, perhaps] that benzazoline may be of value in the diagnosis of this disease.

L. J. Davis

1354. **Pregnancy and Sickle Cell Disease**
J. Q. ADAMS, F. E. WHITACRE, and L. W. DIGGS. *Obstetrics and Gynecology* [*Obstet. Gynec.*] **2**, 335–352, Oct., 1953. 4 figs., 43 refs.

The authors of this important paper from the University of Tennessee College of Medicine describe pregnancy and sickle-cell anaemia as serious mutual hazards. The incidence of the sickle-cell trait without anaemia in 2,011 pregnant negro women was 7·9%, which compares favourably with the figure of 9·4% previously found by one of the authors in a comparable range of the general population. Toxaemia and foetal mortality were increased in women with sickle cells in the blood, but no increased incidence of anaemia occurred. Sickling was found in 1·1% (9 cases) of 824 newborn infants, but none of the infants, including 3 born of mothers with sickle-cell anaemia, had themselves sickle-cell anaemia. Sickle-cell anaemia was found in only one mother out of 2,075 delivered, an incidence lower than that in the general population.

The authors suggest that although fertility is not affected by sickle-cell anaemia, patients with this abnormality die young. The anaemia—as opposed to the sickle trait—is aggravated by pregnancy, and the number of obstetric complications, especially toxaemia and haematuria but not haemorrhage, is increased. It is suggested that although sickle-cell anaemia should not necessarily be considered an indication for abortion or sterilization, labour and delivery must be conducted in such a way as to avoid anoxaemia, severe blood loss, and infection. General, spinal, and caudal anaesthesia should be avoided with any form of sickle-cell disease.

Janet Vaughan

1355. **The Effect of Minimal Doses of Cobalt on Haematopoiesis and Iron Metabolism.** (Die Wirkung kleinster Kobaltgaben auf Blutbildung und Eisenstoffwechsel)
H. DITTRICH. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **78**, 1658–1660, Nov. 27, 1953. 4 figs., 18 refs.

Trials are reported of a new type of cobalt preparation, the sodium salt of cobalt–chlorophyllin, in the treatment of various forms of anaemia at the Evangelical Hospital, Vienna. It is claimed that doses of this preparation containing only 200 to 400 μg. of cobalt are active given intramuscularly, thus enabling the side-effects to be avoided which are liable to arise from the use of existing cobalt preparations, of which much larger doses are necessary. A total of 63 cases of refractory anaemia associated with carcinoma, reticulosis, chronic leukaemia, or infection and 11 cases of unexplained refractory hypochromic anaemia were treated with cobalt–chlorophyllin, with a subsequent increase in erythrocyte count of more than 1,000,000 per c.mm. in 50% of the cases.

A simultaneous significant fall in the leucocyte count is reported in patients suffering from myeloid leukaemia.

During the administration of 200 to 400 μg. of cobalt daily in 7 cases of anaemia the serum iron level fell initially and then rose to normal. This is interpreted as evidence in favour of a complementary action of cobalt and iron in the organism. The mode of action of cobalt is briefly discussed, and mention is made of the possibility of a blocking effect of cobalt on the sulphhydryl groups or its combination with the porphyrin-III ring.

Mary D. Smith

1356. **The Influence of Folic Acid on the Absorption of Iron.** (Der Einfluss der Folsäure auf die Eisenresorption)

H. BEGEMANN, W. KEIDERLING, and F. WALTER. *Klinische Wochenschrift* [*Klin. Wschr.*] **31**, 881–883, Oct. 1, 1953. 4 refs.

The effect of the administration of folic acid on the absorption of alimentary iron was investigated at the University Medical Clinic, Freiburg-im-Breisgau, by plotting the iron absorption curves after the oral administration of ferrous sulphate to 12 normal subjects and 25 patients with anaemia. The anaemic cases studied comprised various types of anaemia including those associated with blood loss, neoplasm, infection, reticulosis, and renal insufficiency, but for the purposes of the present study they were grouped only in regard to whether the total gastric acidity was normal or low.

In the normal subject higher curves were recorded when folic acid was given along with the test dose of ferrous sulphate than when ferrous sulphate was given alone, but the difference was not statistically significant and was apparently unaffected by gastric acidity. In anaemic subjects with low initial serum iron levels and free acid in the gastric juice the apparent increase in absorption of iron when folic acid was added was similar to that in the normal subjects. In anaemic subjects with low acidity, however, much higher serum iron levels were recorded after giving folic acid with ferrous sulphate than after the administration of iron alone. The addition of ascorbic acid to the test dose of iron did not have the same effect. It is concluded that in the presence of low gastric acidity folic acid augments iron absorption, possibly by a direct effect on cell permeability.

Mary D. Smith

NEOPLASTIC DISEASES

1357. **Haematopoiesis and Plasmacytoma.** (Die Blutbildung Plasmocytomkranker)

G. BAYER. *Deutsches Archiv für klinische Medizin* [*Dtsch. Arch. klin. Med.*] **200**, 579–588, 1953. 2 figs., bibliography.

The author describes the haematological features of 36 personal cases of myelomatosis and of 243 cases collected from the literature. In 75% of cases the erythrocyte count was less than 4,000,000 per c.mm., and the anaemia was most marked in the rapidly progressive cases. Leucopenia was uncommon and usually occurred only in the later stages of the disease. Plasma cells also appeared in the peripheral blood only at a late stage, and never in very great numbers (27 to 3,250 per c.mm.). There was often some reduction in the platelet count.

P. C. Reynell

1358. **Treatment of Leukemia with Triethylene Thiophosphoramide (Thio-TEPA). Preliminary Results in Experimental and Clinical Leukemia**

H. SHAY, C. ZARAFONETIS, N. SMITH, I. WOLDOW, and D. C. H. SUN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **92**, 628–645, Nov., 1953. 9 figs., 15 refs.

Rats with experimentally induced acute or chronic myelogenous leukaemia were treated with triethylene thiophosphoramide (" thio-TEPA "). This drug induced remissions in the chronic form, but failed to alter the course of the acute disease. Encouraged by this the authors administered thio-TEPA to 49 human patients, 39 with malignant disease originating in the haematopoietic system and 10 with other inoperable malignant lesions. The drug was supplied as a solution in sterile isotonic saline in a concentration of 10 mg. per ml. and was given intramuscularly or intravenously in doses of 2, 5, or 10 mg. Intramuscularly the drug was given in undiluted solution, but for intravenous administration it was diluted with an equal volume of saline and injected over a period of 2 minutes. Injections were given daily or at longer intervals, and later the drug was given by mouth in doses of 10 to 30 mg. The route and dosage were determined by the haematological findings.

In man as in the experimental animal thio-TEPA appeared to act most favourably as a suppressive drug in subacute and chronic leukaemia and in Hodgkin's disease, inducing remissions lasting up to 6 months. In lymphosarcoma it seemed less effective, and in acute leukaemia the results were most discouraging. Of the 10 patients with inoperable malignant disease, 2 with recurrent and metastatic adenocarcinoma of the breast showed striking objective improvement. The drug is remarkably free from immediate toxic effects, and undue bone-marrow depression is readily reversed by temporarily withholding treatment.

Thio-TEPA has been used for only 6 months so far, but in the authors' opinion it gives promise of being very useful in the chemotherapy of malignant disease.

E. G. Rees

1359. **Haemorrhage in Myeloid Leukaemia.** (Les hémorragies des leucémies myéloïdes)

P. CHEVALLIER. *Bulletin de l'Académie nationale de médecine* [*Bull. Acad. nat. Méd. (Paris)*] **137**, 528–533, Nov. 3, 1953.

The author discusses the cause of the haemorrhage which occurs in chronic myeloid leukaemia with reference to 138 cases of the condition in 76 males and 62 females ranging in age from 13 to 71 years. In 20% of the cases haemorrhage was the presenting symptom, and was seen slightly more often in females. In one-third of these cases the haemorrhage was first noticed after injury of a fairly definite kind, such as surgical operation or dental extraction; in another third the injury was very slight, and in the remaining third the

haemorrhage was apparently spontaneous. Patients presenting with haemorrhage were no more likely to bleed at a later stage than those with other initial signs.

During the period of observation 47 patients died. In about half of these cases haemorrhage, not necessarily severe, occurred in the final stages. Bleeding was most common from the rectum, mouth, or into the skin, but was noted in a wide variety of situations. Very often haemorrhage was first seen 1 or 2 months before death, but not infrequently it began to occur 6 months to one year before. Observation of those who underwent splenectomy suggested that this operation does not improve the condition, but rather encourages any tendency towards haemorrhage.

In patients without haemorrhage, estimation of the bleeding time and coagulation time gave normal values, while in some the prothrombin time was even reduced. In certain patients in whom localized haemorrhage had occurred on isolated occasions the tests also gave normal values; possibly these haemorrhages were due to leukaemic infiltration of the tissues. In haemorrage in the terminal stages clot retraction was often poor and the bleeding time commonly prolonged, but the number of platelets was frequently increased. Clot retraction time may be normal in cases with severe haemorrhage, and in one case in which prothrombin time was prolonged the administration of vitamin K intravenously produced great, although only temporary, improvement. *T. M. Pollock*

BLOOD TRANSFUSION

1360. **Defective Gas-transport Function of Stored Red Blood-cells**

D. J. VALTIS and A. C. KENNEDY. *Lancet* [*Lancet*] **1**, 119–125, Jan. 16, 1954. 7 figs., 39 refs.

At the Royal Infirmary, Glasgow, a study was made of the oxygen and carbon dioxide dissociation curves of stored blood from a blood bank or obtained from volunteers, and of the oxygen dissociation curve of blood from 10 recipients of such blood before and after transfusion. Over 100 samples of blood were examined, some of which had been stored for as long as 90 days, though most of the observations were made on blood stored up to 20 days, by which time the changes observed were fully developed.

With blood stored with standard acid citrate dextrose (A.C.D.) anticoagulant medium the oxygen dissociation curve showed a progressive shift to the left, indicating a reduced ability to liberate oxygen to the tissues, and at the same time the amount of carbon dioxide released for each volume per cent. of oxygen saturation of haemoglobin was reduced. Blood stored for 7 days with either trisodium citrate or acid heparin showed similar changes but to a lesser degree. With heparin fluoride no such changes were observed in samples stored up to 7 days, after which time haemolysis became severe. Buffered solutions of laked blood prepared from citrated blood stored 20 days gave oxygen dissociation curves identical with those given by solutions prepared from fresh blood. The changes were small in blood stored with A.C.D. for one day, much larger after 7 days, and even greater after 20 days' storage.

These findings were confirmed in studies of the blood of recipients, the oxygen dissociation curve of which showed a temporary shift to the left which was proportional in degree to the amount of blood transfused and the length of storage. Thus a small transfusion of 1 pint (0·6 litre) of fresh blood did not appear to alter the dissociation curve, whereas transfusion of 2 pints (1·1 litre) of 20-hour-old blood caused a slight shift to the left, and when 2 or 3 pints (1·1 or 1·7 litres) of 7-day-old blood was given the dissociation curve was substantially shifted to the left immediately after transfusion. The effect upon the recipient's blood did not appear to increase, however, when blood more than 7 days old was given. The alteration in the oxygen dissociation curve in the recipient's blood remained for several hours, and slight abnormality was detectable for several days.

An example of the clinical effect of this alteration is given in the case of a patient with a haemoglobin value of 35% who received 3 pints (1·7 litres) of blood which had been stored for 1 to 2 weeks. Although the haemoglobin value rose to 55%, the shift of the oxygen dissociation curve to the left was such that after transfusion the patient's blood could not give up to the tissues as much oxygen as it did before. *John Murray*

1361. **Intra-arterial and Intravenous Transfusion. A Controlled Study of their Effectiveness in the Treatment of Experimental Hemorrhagic Shock**

J. V. MALONEY, C. MCC. SMYTHE, J. P. GILMORE, and S. W. HANDFORD. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **97**, 529–539, Nov., 1953. 12 refs.

Experiments were carried out on 64 dogs to determine the relative effectiveness of intravenous and intra-arterial blood transfusion in the treatment of haemorrhagic shock. No evidence was obtained that intra-arterial transfusion was any more or less effective than intravenous transfusion. Recovery of arterial and venous pressure after shock was unrelated to the route of transfusion; both routes were equally effective in restoring to normal the low cardiac output characteristic of haemorrhagic shock.

To determine the effect of intra-arterial transfusion on the coronary blood flow, radiographs were taken after injection of a radio-opaque substance (" skiodan ") into various arteries. Normally, no filling of the coronary arteries was observed, but when cardiac output ceased during ventricular fibrillation the coronary arteries filled with skiodan. Experiments on 26 animals failed to reveal any significant difference in the survival rate between those given intra-arterial transfusion and those given intravenous transfusion. The authors point out that intra-arterial transfusion under pressure carries with it the risk of ischaemia, necrosis of the extremities, pain, and air embolism. Further, while intra-arterial transfusion may, on theoretical grounds, be the route of choice when the output of blood from the left heart has ceased, the time required for cutting down on the artery involves a delay which counteracts the possible advantages of this method. *Kate Maunsell*

Respiratory System

1362. **Congenital Anterior Chest Wall Deformities of Diaphragmatic Origin**
H. A. BRODKIN. *Diseases of the Chest* [*Dis. Chest*] **24**, 259–277, Sept., 1953. 10 figs., 14 refs.

Evidence is presented in support of the author's view that the three deformities of the anterior chest wall known as " funnel chest ", " pigeon chest ", and " Harrison's grooves " are congenital and are produced by the abnormal inspiratory contraction of an abnormally developed diaphragm. In such cases the anterior portion of the diaphragm is deficient in muscular fibres and thus on contraction is pulled down with the membranous portion; this effects a pull on the anterior chest wall during inspiration.

Funnel chest, for which the term " congenital chondrosternal depression " is proposed, is due to this mechanism and not to a short central tendon as has been suggested. Cardiac symptoms, when severe, may be relieved by surgical treatment, the technique of which is described.

Pigeon chest, which the author terms " congenital chondrosternal prominence ", is produced in the same way, the difference being in the character and composition of the anterior portion of the diaphragm. At necropsy on an infant with this deformity the anterior membranous portion of the diaphragm was found to be V-shaped and the anterior muscular part poorly developed; the lateral portions were unusually muscular. This had the effect of producing an inspiratory retraction of the lower portion of the anterior chest wall.

Discussing the mechanism of Harrison's grooves, the author points out that transitory inspiratory retractions along the sixth costal cartilage may be seen in normal infants during crying spells, because the weakest and most yielding part of the diaphragm is attached to the sixth costal cartilage almost perpendicularly, with no costophrenic sinus; thus there is an immediate pull at this point. If the anterior part of the muscular segment is deficient in muscle, retraction will occur on quiet respiration. It is suggested that the term " congenital chondrocostal grooves " should replace the term " Harrison's grooves ". *T. M. Pollock*

LUNGS AND BRONCHI

1363. **Eosinophils in the Sputum**
J. VAUGHN. *British Medical Journal* [*Brit. med. J.*] **1**, 27–28, Jan. 2, 1954. 18 refs.

The author observed that specimens of sputum from natives in Tanganyika often contained eosinophil leucocytes; eosinophilia in the blood, which frequently accompanies a high incidence of parasitic diseases, was also common. Examination of sputum and peripheral blood from 205 African natives showed that, in general, the higher the eosinophilia in the blood the greater the density of eosinophils in the sputum. However, this relationship was not observed in approximately one-quarter of the subjects, no eosinophils being found in the sputum of some subjects with a high eosinophilia, while numerous eosinophils were found in the sputum of subjects without eosinophilia. The author suggests that eosinophilia first appears in the blood, then infiltrates lung tissue, and so reaches the sputum. This sequence may take some time, which would account for the observed discrepancies. *Arthur Willcox*

1364. **Finger Clubbing and Changes in the Bronchial Circulation**
L. CUDKOWICZ and J. B. ARMSTRONG. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **47**, 227–232, Oct., 1953. 5 figs., 23 refs.

To determine whether pulmonary vascular abnormalities are present in patients with intrathoracic disease accompanied by clubbing of the fingers the authors, at the Postgraduate Medical School of London, examined the bronchial circulation in a variety of such diseases. Soon after death a radio-opaque medium which was too coarse to penetrate vessels of less than 60 μ in diameter was injected into the bronchial arteries (by a method described in a previous paper by the authors (*Thorax*, 1951, **4**, 343)). By this means it was possible to obtain radiographs of the thoracic contents before histological examination was carried out. The lungs of 15 subjects were examined in this way.

Radiologically, varying degrees of bronchopulmonary anastomosis were observed. Histological examination showed that in 14 of the 15 cases the pulmonary artery was occluded proximal to the anastomosis. Beyond the occlusion the vasa vasorum were dilated and recanalized the occluded lumina, thus establishing contact with the patent peripheral pulmonary arterioles. The proximal bronchial arteries were enlarged, and the smaller peripheral bronchial branches showed narrowing of their lumina.

These observations suggest that in severe diseases of the lung, clubbing of the fingers and bronchopulmonary anastomosis co-exist, but whether clubbing can be related causally to the bronchopulmonary anastomosis is uncertain, as it occurs in other diseases, such as cirrhosis of the liver. *T. M. Pollock*

1365. **Further Observations on Smoker's Respiratory Syndrome**
G. L. WALDBOTT. *Annals of Internal Medicine* [*Ann. intern. Med.*] **39**, 1026–1031, Nov., 1953. 6 refs.

The diagnosis of " smoker's asthma " depends on the presence of the triad of (1) chronic pharyngitis, (2) wheezing and dyspnoea, and (3) recurrent respiratory infections. The most characteristic of these is the first. Chest pains and precordial constriction are commonly

associated with the syndrome. The wheezing is less severe than in asthma and originates principally in the tracheobronchial area. Throat infections are common. The nose is healthy and the classic allergic oedema of the nasal mucosa is absent. Similarly the bronchial mucosa is red and inflamed and there is little true bronchospasm. It would appear that the diagnosis is most easily made retrospectively, when cure follows the cessation of smoking. Where infection predominates, antibiotics must also be used. A series of 58 cases is described, in 34 of which the patient recovered completely upon cessation of smoking and in 24 upon the addition of antibiotic treatment.

[While smoking is well recognized as a pharyngeal, laryngeal, and bronchial irritant, most people will agree that it is unnecessarily artificial and strained to delineate a separate syndrome.] *Ronald S. McNeill*

1366. **The Relationship between Pulmonary Function and the Pulmonary Circulation.** (Beziehungen zwischen Lungenfunktion und Lungenkreislauf)

A. BÜHLMANN, C. MAIER, M. HEGGLIN, R. KÄLIN, and F. SCHAUB. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **83**, 1199–1202, Dec. 12, 1953. 3 figs., 25 refs.

The authors, working at the University Polyclinic, Zürich, have studied the relationship between pulmonary hypertension and respiratory function, and in particular the effect of changes in alveolar oxygen and carbon dioxide tension on the pulmonary arterial pressure, in a variety of respiratory and cardiac conditions. [The methods employed are not stated.] On the basis of their findings they distinguish four groups, the characteristics of which are described as follows.

(1) Certain congenital cardiovascular abnormalities: persistent ductus arteriosus, ventricular septal defect, Eisenmenger's complex, and pulmonary arterio-venous aneurysm. In these cases the cardiac output is high and exercise tolerance good. Respiratory function is generally normal, and the pulmonary arterioles and capillaries are normal (with the possible exception of the Eisenmenger complex). Arterial oxygen unsaturation due to the presence of a shunt is the cause of dyspnoea in this group.

(2) Mitral stenosis causes pulmonary congestion and hypertension from obstruction at the distal end of the lesser circulation. Pulmonary arterial pressure may be further raised by reflex constriction of the pulmonary vessels. When congestion is marked, respiratory function suffers even at rest, and poor exercise tolerance is characteristic. After valvotomy the pulmonary arterial pressure may fall, but congestion remains if there is any mitral insufficiency. Early postoperative pulmonary function tests do not constitute a reliable prognostic guide. To this group also belongs pulmonary hypertension from a failing left ventricle.

(3) Massive reduction in the capillary bed (pulmonary sclerosis) may be either primary or secondary. Pulmonary arterial pressure is increased and the capillary surface area decreased. The time of contact between blood and alveolar gases is therefore reduced, causing a high degree of oxygen unsaturation and dyspnoea at rest. Carbon dioxide, being highly soluble, is given off normally, and hyperventilation causes a reduction in arterial carbon dioxide values. Pulmonary sclerosis should be suspected in the absence of a right-to-left shunt when the alveolar–arterial oxygen difference is markedly increased. Pulmonary function is seriously impaired, though alveolar ventilation is normal. Since pneumonectomy does not result in a similar degree of disability it is thought that at least two-thirds of the pulmonary capillary bed must be affected to give the clinical picture of pulmonary sclerosis. Secondary pulmonary sclerosis occurs in rare cases of emphysema from destruction of the alveolar septa and capillary obliteration. In these cases alveolar ventilation is inadequate, arterial oxygen saturation decreased, and arterial carbon dioxide saturation increased (" global insufficiency ").

(4) In cases of emphysema with kyphoscoliosis " global insufficiency " is present, yet the capillary bed is normal. It is concluded that chronic alveolar hypoventilation raises the pulmonary arterial pressure before cardiac or pulmonary vascular changes have occurred.

Electrocardiographic findings are described and a table summarizing the experimental data in 12 illustrative cases is appended.

[This interesting article may help to clarify a somewhat confused subject. Some of the authors' assumptions are debatable—for example, that oxygen unsaturation in pulmonary sclerosis is due to a reduced blood–gas contact time, and that oxygen lack is the cause of dyspnoea in Eisenmenger's complex.] *F. Starer*

1367. **The Pulmonary Alveolar Epithelium of Laboratory Mammals and Man**

F. N. LOW. *Anatomical Record* [*Anat. Rec.*] **117**, 241–263, Oct., 1953. 9 figs., 20 refs.

The author describes a study carried out at Louisiana State University School of Medicine, New Orleans, of the micro-histology of the pulmonary alveolar epithelium as observed in material taken from living laboratory animals under non-inhalation anaesthesia (and in one case from a human subject at pneumonectomy), fixed in 1% osmic acid for 4 hours, embedded in methacrylate, cut in sections 0·06 μ thick with a glass knife, and examined under the electron microscope. Much of the paper is devoted to a discussion, illustrated by diagrams, of the difference between the appearance of a section under the light microscope and that seen under the electron microscope. Under the electron microscope the depth of focus is about 10 times greater than the smallest particle resolved, with the result that in the examination of sections of a thickness suitable for electron microscopy, every structure in the field appears in sharp focus at its maximum size. Thus the identification of objects such as protoplasmic and basement membranes is only possible when they are lying vertically in the electron beam. The author suggests that the different opinions which have been expressed regarding the existence of a pulmonary alveolar epithelium have been due largely to the difficulty of identifying such fine structures by means of the light microscope.

From a study of his preparations [of which adequate illustrations are given] the author concludes that the lung alveoli are lined with a continuous cellular epithelium, broken only when free cells (alveolar macrophages) penetrate it. The nuclei of the epithelial cells are surrounded by a mass of cytoplasm countersunk in the alveolar wall. From the edge of the mass containing the nucleus a thin cytoplasmic extension covers the wall of the alveolus and is continuous with extensions from neighbouring epithelial cells. Both this epithelial lining and the endothelial lining of the capillaries possess a thin basement membrane. *R. P. Foggie*

1368. **Chloramphenicol Treatment of Bronchiectasis in Children**
A. W. FRANKLIN and L. P. GARROD. *British Medical Journal* [*Brit. med. J.*] **2**, 1067–1069, Nov. 14, 1953.

The authors describe their experience with chloramphenicol in the treatment of 36 children suffering from bronchiectasis at St. Bartholomew's Hospital, London. The sputum from all but one of these children contained *Haemophilus influenzae*; in 10 cases *Streptococcus pneumoniae* was present as well. From the sputum of the remaining patient a pure growth of pneumococci was obtained.

The minimum effective daily dose of chloramphenicol was 20 mg. per lb. (44 mg. per kg.) body weight. There was a reduction in the quantity of sputum, which, after 3 or 4 days, became sterile and mucoid. Prolonged treatment was sometimes accompanied by an increase in the quantity of mucoid sputum despite the absence of pus and bacteria. Patients with mild unilobar bronchiectasis remained symptom-free for many months, in some instances as long as one year. Those with severe bronchiectasis relapsed within 10 days of cessation of treatment, *H. influenzae* again being found in the sputum; the relapse was sometimes preceded by a mild febrile illness lasting one or two days.

Unfortunately one patient died from aplastic anaemia (one similar, unpublished, case is mentioned); the authors therefore consider that the possible toxic effects of chloramphenicol on the bone marrow make prolonged treatment unwise. While recognizing the need in bronchiectasis for a drug with the therapeutic value of chloramphenicol, they do not intend to persist with this treatment. *A. Gordon Beckett*

1369. **Chronic Bronchitis in General Practice**
J. FRY. *British Medical Journal* [*Brit. med. J.*] **1**, 190–194, Jan. 23, 1954. 13 refs.

The incidence of, and morbidity from, chronic bronchitis in a general practice in a suburb of London during the year 1952 are discussed. Of the 4,500 patients in the practice, 127 (71 males and 56 females) suffered from chronic bronchitis, the disease accounting for 8% of all attendances during the year. The incidence of bronchitis rose with age, the onset generally being between the ages of 30 and 60; two-thirds of the patients had had the disease for more than 10 years. Most of the patients in the practice were in Social Classes 3 and 4, being employed in light industry or in clerical and administrative duties, and the incidence of chronic bronchitis reflected this distribution. No difference was found between the smoking habits of patients with bronchitis and those of a control group. Nearly one-third of the patients were incapacitated by bronchitis for more than one month in the year, while 12% were classified as complete invalids. It is suggested that further study of the aetiology of this disease and of the causes of regional variation in its incidence is necessary.

[The author is to be congratulated on preparing this valuable report under the exacting conditions of general practice.] *Bernard Isaacs*

1370. **Treatment of Pneumococcal Pneumonia with Erythromycin and Carbomycin (Magnamycin)**
P. A. BUNN and E. COOK. *Archives of Internal Medicine* [*Arch. intern. Med.*] **92**, 333–340, Sept., 1953. 2 figs., 11 refs.

Erythromycin (12 cases) and carbomycin (8 cases) were used in the treatment of proved pneumococcal pneumonia at the Syracuse Medical Center Hospitals, New York. Of the 20 patients, 15 were acutely ill and 5 critically so.

Erythromycin was given by mouth in doses of 1·2 to 2 g. daily over a period of 1 to 12 days. Five of the 12 patients responded well, 4 had delayed resolution (which is defined as the presence of residual clinical or radiological signs 3 weeks after the start of treatment), 1 failed to respond until penicillin was given, and 2 patients died.

Carbomycin was given either by mouth or by intramuscular injection in doses of 1·25 to 2 g. daily over a similar period. The response was satisfactory in 4 cases, delayed resolution occurred in 1, and failure to respond occurred in 3 cases. There were no deaths in this group.

It is concluded that erythromycin and carbomycin should not be used in the treatment of pneumococcal pneumonia. *Keith Ball*

1371. **Ineffectiveness of Aureomycin in Primary Atypical Pneumonia. A Controlled Study of 212 Cases**
S. H. WALKER. *American Journal of Medicine* [*Amer. J. Med.*] **15**, 593–602, Nov., 1953. 4 figs., 15 refs.

In a controlled study of 212 cases of " primary atypical pneumonia " undertaken at the William Beaumont Army Hospital, Fort Bliss, Texas, the patients were given either aureomycin or a placebo. Repeated cultures of sputum and of the flora from the throat were made in order to exclude bacterial pneumonia, and serological tests were performed to exclude Q fever and psittacosis. A fourfold rise in titre of cold haemagglutinins was noted in half those cases which showed radiological evidence of pneumonia.

Comparison of the average duration of the symptoms and signs in the two groups showed no significant difference between them, and the author therefore concludes that, contrary to previous reports, aureomycin is ineffective in primary atypical pneumonia.

[In the abstracter's opinion the data provided are insufficient to justify so sweeping a conclusion. The diagnostic criteria adopted are not defined (although the

author has succeeded in introducing the meaningless term "typical atypical pneumonia") and the radiographic appearances and serological findings, which are of major diagnostic importance in this disease, are hardly mentioned. Moreover, it would appear that steps were not taken to exclude serologically the possibility of influenzal pneumonia, while aspiration pneumonia following an infection of the upper respiratory tract was not considered as an alternative diagnosis; both these conditions may be resistant to aureomycin.]

D. Geraint James

1372. **The Superior Vena Cava Obstruction Syndrome in Bronchogenic Carcinoma. Pathologic Physiology and Therapeutic Management**

B. ROSWIT, G. KAPLAN, and H. G. JACOBSON. *Radiology* [*Radiology*] **61**, 722–737, Nov., 1953. 8 figs., 25 refs.

The authors discuss the physiology, pathology, and treatment of the syndrome arising from the increasing obstruction of the superior vena cava caused by bronchial neoplasm, with special reference to 38 patients in whom this syndrome was due to bronchial carcinoma and who were treated at the Veterans Administration Hospital, Bronx, New York, by irradiation and with nitrogen mustard. The syndrome is relatively frequent and occurred in some 15% of all cases of bronchial carcinoma seen by the authors. In about 80% of cases the growth arises from the right main or upper-lobe bronchus, and the obstruction is usually associated with rapidly growing, anaplastic types of tumour. When it is above the azygos vein it is tolerated better than when it is below, for in the latter case the collateral circulation (which is extensively developed in all cases) is more circuitous and less efficient. Exact diagnosis of the site of obstruction can be made by means of phlebography or angiocardiography, and routine angiocardiography in cases of bronchial carcinoma may demonstrate early obstruction of the vein before there are symptoms or physical signs of it. This is an ominous finding, for it shows that the growth has become inoperable, but it may at least prevent the performance of a useless thoracotomy.

Details are given of the authors' irradiation technique, in which the hardest quality of *x* radiation available was employed; up to 250 r daily was given, and 20 patients received 28 courses, in 21 (75%) of which a satisfactory response was obtained. The average remission period was 14 weeks, and in 6 patients the remission lasted from 6 to 12 months. Nitrogen mustard was given in a dose of 0·1 mg. per kg. body weight by injecting it through the rubber tubing of the apparatus during an intravenous infusion of saline in order to lessen the danger of causing phlebitis. The dose was repeated on each of four successive days. Only 8 patients received this form of treatment, in a total of 15 courses, of which 12 (80%) produced a satisfactory remission, which, however, lasted an average of only 7 weeks, in 4 instances being less than 1 month but in 8 from 1 to 5 months. Four patients were treated with both *x* irradiation and nitrogen mustard, but the results of this combined treatment were not strikingly better than those obtained with irradiation alone.

It is concluded that irradiation is the treatment of choice for this distressing syndrome. No claim is made that life is prolonged thereby, but considerable palliation is usually achieved. In no case of the present series did irradiation in an average total dose of 3,600 r produce any untoward effects, and its risk therefore seems to be slight. In the authors' view nitrogen mustard therapy should be given only in intervals when *x*-ray treatment is not feasible or is ineffective, but when so employed it can be a valuable adjunct to treatment.

John R. Forbes

1373. **Clinical Follow-up Study of 398 Patients Suspected of Having Lung Cancer Discovered in the Boston Chest X-ray Survey**

J. M. MCNULTY. *New England Journal of Medicine* [*New Engl. J. Med.*] **250**, 14-17, Jan. 7, 1954. 1 ref.

1374. **Surgical Treatment of Bullous Emphysema. Contributions of Angiocardiography**

L. MISCALL and R. W. DUFFY. *Diseases of the Chest* [*Dis. Chest*] **24**, 489–499, Nov., 1953. 6 figs., 9 refs.

Diagnostic methods which facilitate recognition of bullous emphysema and the surgical treatment of this condition are discussed in this paper from the New York Hospital—Cornell Medical Center. Three types of bullous emphysema may require surgical treatment: localized cysts or bullae, diffuse emphysema of a lobe, and small blebs causing recurrent pneumothorax. Check-valve obstruction of a bronchus, resulting in compression of a lung already impaired by emphysema, may lead to serious dyspnoea. Surgery is of help when it is possible to resect irreversibly damaged tissue and allow the remaining compressed lung to expand; dramatic relief of symptoms can often be achieved. Exact delineation of the extent of the bullous change is essential; for this angiocardiography is reliable. In emphysematous areas vessels are reduced in size and number proportionately to the distension; in advanced cases they may be totally absent. Vessels fill poorly and are crowded in compressed lung; after operation with re-expansion the pattern returns to normal. Corresponding data are found by bronchography, but this procedure in patients with lowered ventilatory reserve carries a greater risk and is not recommended.

Elective surgical treatment is indicated when pulmonary function is significantly reduced by a localized lesion and when improvement can be expected after expansion of compressed lung, even if symptoms are not severe. In the treatment of chronic pneumothorax excision of blebs is preferred to induction of chemical pleuritis. Concomitant decortication may be necessary. The line of excision may not follow an anatomical plane, and careful repair of all bronchial leaks is essential. Multiple-tube drainage with prolonged suction is necessary. To avoid over-expansion of remaining lung after extensive resection, reduction of thoracic volume is indicated. The authors prefer to do this by constructing a pleural tent, made by mobilizing the apical pleura and suturing it to the operative wound, rather than by thoracoplasty.

M. Meredith Brown

Otorhinolaryngology

1375. **Basal-cell Carcinoma of the External Auditory Canal and Middle Ear**
H. BRUNNER. *Archives of Otolaryngology* [*Arch. Otolaryng. (Chicago)*] **58**, 665–676, Dec., 1953. 4 figs., 20 refs.

Carcinoma of the ear is not a common condition, and of the cases reported, about one-third have been of the basal-cell type (this term being used here to include all tumours that are supposed to originate in the basilar layer of the epidermis and its appendages or in the salivary glands). Rodent ulcer—the commonest basal-cell skin carcinoma elsewhere—is infrequent in the auditory canal.

The author reports 3 cases of basal-cell carcinoma of the ear, of which he distinguishes two different types. (1) The more common type arises in the external canal from the basilar layer of the epidermis or from the sweat glands. The growth is firm, even hard. It grows slowly and usually does not invade cartilage, but may attack the bone. Pain and deafness are the usual symptoms; excessive bleeding is rare. Invasion of the tympanic cavity is late. Metastases do not form. The treatment is by surgical excision and irradiation. (2) The less common basal-cell carcinoma of the middle ear probably arises from aberrant portions of the parotid gland lying in the floor of the middle ear. It is not a glomus tumour, although it is located in the same area. It has a glandular appearance, not that of a paraganglion. It has no nerve supply and few blood vessels. It is contained in a connective-tissue capsule, and has no connexion with the petrosal nerve. It may lie latent in the hypotympanum for a long time before it breaks through the tympanic membrane or into the facial canal. Eventually it becomes infected and may metastasize. Treatment consists in surgical excision, often with radical dissection of the neck and irradiation. Cures lasting several years have been reported.

F. W. Watkyn-Thomas

1376. **Rostral Projection Pathway of the Vestibular System**
W. A. MICKLE and H. W. ADES. *American Journal of Physiology* [*Amer. J. Physiol.*] **176**, 243-246, Feb., 1954. 4 figs., 13 refs.

1377. **Avoidable Failures in the Treatment of Carcinoma of the Tonsil.** (Vermeidbare Misserfolge bei der Behandlung des Tonsillen-Karzinoms)
H. TRÜBESTEIN. *Strahlentherapie* [*Strahlentherapie*] **91**, 194–207, 1953. 18 refs.

The results of treatment in 60 cases of carcinoma of the tonsil are analysed in this paper from the University Röntgen Institute, Frankfurt-am-Main. Of these cases, 17 were treated by a combination of surgery and post-operative radiotherapy, and 5 of these patients have survived symptom-free for over 5 years. The remaining 43 patients were treated exclusively by external *x*-ray therapy, supplemented in some cases by intraoral Chaoul treatment and/or interstitial radium therapy. Of this group, only one patient survived without symptoms for 5 years. The period of survival in the remainder appeared to depend mainly on three factors: (1) the state of advancement of the disease; (2) the histological grading of the tumour; and (3) the radiation dosage; in other words, the smaller and more differentiated the tumour and the higher the radiation dose given, the longer, in general, was the period of survival without symptoms.

Jan G. de Winter

1378. **Closure of the Larynx**
G. M. ARDRAN, F. H. KEMP, and L. MANEN. *British Journal of Radiology* [*Brit. J. Radiol.*] **26**, 497–509, Oct., 1953. 9 figs., 7 refs.

In a study of the alterations in the lumen of the larynx during breathing and phonation carried out at the Nuffield Institute for Medical Research, University of Oxford, 200 normal subjects were examined by cine-radiography, still radiography, and tomography, and 20 hospital patients after the introduction of iodized oil. On quiet respiration the larynx was wide open, its lumen being very little less than that of the trachea. The vocal folds were withdrawn and usually turned up over the laryngeal ventricles, so that their free edges were closely approximated to the lower surfaces of the false cords. The central axis of the airway was bent backwards on the trachea to an angle of 30 to 40 degrees. There was very little movement of the larynx on quiet respiration. Voluntary cessation of breathing was usually associated with partial closure of the airway, but in some subjects there was approximation of the vocal folds, obliteration of the ventricles, and apposition of the ventricular folds, two methods of approximation of the vocal folds being observed: (1) the lumen was constricted and the up-turned folds brought together; or (2) the lumen remained the same, but the folds turned down and their free edges were brought together. There was a little shortening of the antero-posterior diameter of the larynx.

Phonation was associated with a variable degree of closure. The act of closure began before a sound was heard, the larynx being then partially closed, or completely closed and then partially opened. Partial closure in preparation for speech was sometimes sustained for several seconds. During speech there was sustained activity of the vocal, vestibular, and aryepiglottic folds. If a single sound was maintained at an even intensity, the size of the lumen and shape of the larynx remained constant. In singing the whole larynx vibrated.

The authors point out that these findings differ somewhat from the well-known views of Negus (*Comparative Anatomy and Physiology of the Larynx*, London, 1949).

S. A. Beards

Endocrinology

THYROID GLAND

1379. **Calorigenic and Antigoitrogenic Actions of L-Triiodothyronine and L-Thyroxine in Thyroidectomized and Intact Rats**

A. E. HEMING and D. E. HOLTKAMP. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **83**, 875–879, Aug.–Sept., 1953. 3 figs., 7 refs.

The antigoitrogenic effects of 3:5:3′-L-triiodothyronine and L-thyroxine sodium pentahydrate were compared in male albino rats given these substances either in the intact state or 30 or more days after thyroidectomy. Triiodothyronine was about 3·5 times as active as thyroxine, on a molar basis, in inhibiting the goitrogenic effect of thiouracil, as shown by the relative weights of the thyroid glands expressed as mg. per 100 g. body weight.

The molar potency ratio of L-triiodothyronine to L-thyroxine, as measured by the change in oxygen consumption in thyroidectomized animals and compared with that of controls, was approximately 3·5 to 1 within the hypothyroid and euthyroid ranges, but was even greater in the hyperthyroid range. The effects of triiodothyronine on oxygen consumption in intact rats were, however, little different from those of thyroxine when given in dosage ratios of 1 to 1 or 1 to 3·5.

The results are in agreement with those of Gross and Pitt-Rivers (*Lancet*, 1952, **1**, 593).

Robert de Mowbray

1380. **A Comparison of the Metabolic Activities of 3:5:3′-L-Triiodothyronine and L-Thyroxine in Myxedema**

S. P. ASPER, H. A. SELENKOW, and C. A. PLAMONDON. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **93**, 164–198, Sept., 1953. 12 figs., bibliography.

In metabolic studies carried out at the Johns Hopkins University School of Medicine, Baltimore, 3 patients with classic myxoedema were kept on a constant diet calculated to maintain approximate nitrogen equilibrium and given successively either 3:5:3′-L-triiodothyronine or L-thyroxine subcutaneously. The basal metabolic rate was, wherever possible, allowed to return to its original level after the administration of one compound before changing to the other. The order of administration of the two compounds was alternated.

L-Triiodothyronine produced all the clinical and metabolic effects of L-thyroxine, but in much greater degree. Subcutaneous injection of L-triiodothyronine led to increased warmth of the skin and a rise in temperature and pulse rate within 4 to 6 hours and an increase in mental alertness and physical activity within 24 hours. There was an increase in urinary output, a loss of oedema and of body weight, and a slight increase in sweating. No comparable effects were achieved with equimolar doses of L-thyroxine, though there was a slight diuresis and some loss of body weight. The increase in oxygen consumption was 5 to 10 times greater with L-triiodothyronine than with L-thyroxine, and the increases in total urinary nitrogen and creatine output were also greater. The blood non-protein nitrogen level was slightly raised (up to 86 mg. per 100 ml.) during periods of rapid increase in metabolic rate, reflecting the rapid catabolism of body protein. Urinary phosphorus excretion was markedly increased under the influence of both compounds, but in contrast to findings of other workers urinary and faecal calcium excretion was diminished rather than increased.

Improvement in the electrocardiographic T waves occurred more rapidly with L-triiodothyronine than with L-thyroxine. In one patient, in whom slight overdoses of thyroid were known to initiate bouts of paroxysmal tachycardia, L-triiodothyronine induced these episodes in smaller doses than did L-thyroxine.

The level of serum protein-bound iodine after 3 days' treatment with L-triiodothyronine was far less than might have been expected from the rise in oxygen consumption, while the rise in these levels after treatment with L-thyroxine were proportionately greater, even though the patients remained hypothyroid. The change in the levels of protein-bound iodine caused by triiodothyronine would theoretically be expected to be only 75% of that of an equivalent amount of thyroxine, since the former contains three atoms and the latter four atoms of iodine per molecule. Even so, the higher levels of protein-bound iodine with L-thyroxine and the more powerful metabolic effects of L-triiodothyronine, together with other experimental evidence, suggest that the presence of thyroxine in the circulating blood represents a reservoir of thyroid hormone for transformation to triiodothyronine, and that the latter is probably the tissue form of the thyroid hormone. *Robert de Mowbray*

1381. **The Physiologic Activity of L-Triiodothyronine**

J. LERMAN. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **13**, 1341–1346, Nov., 1953. 1 fig., 7 refs.

The author describes a trial of L-triiodothyronine in the treatment of 5 patients with myxoedema at the Massachusetts General Hospital, Boston, the dosage of the drug being 0·1 mg. daily intravenously. The curve of the basal metabolic rate, which was estimated in 4 of the patients, rose to the same extent as the standard curve of response to the intravenous administration of thyroxine polypeptide (1 mg. daily) or of L-thyroxine (0·4 mg. daily), indicating that the compound was 4 to 5 times more active than thyroxine. The clinical effects and the changes in the serum cholesterol level were also similar to those observed with 4 to 5 times the dose of L-thyroxine. There was a difference, however, in the

effect on the serum protein-bound iodine concentration: when treatment with triiodothyronine ceased the protein-bound iodine content of the serum fell to pre-treatment levels within 16 to 36 hours whereas it remained at euthyroid level for several days after administration of thyroxine ceased. This rapid reversal of the effect of treatment with triiodothyronine was also seen in the basal metabolic rate, which fell to the pre-treatment level in 7 to 9 days; the period after cessation of thyroxine treatment was 50 to 70 days. It was also found that a single intravenous dose of 0·1 or 0·2 mg. of triiodothyronine caused little change in the serum protein-bound iodine concentration within 24 hours, whereas there was an appreciable rise 6 hours after injection of 0·2 or 0·4 mg. of thyroxine; this difference could not be explained by variation in urinary iodine excretion.

The author interprets the results as follows. Triiodothyronine is the active thyroid hormone; it is rapidly absorbed into the tissue cells and quickly metabolized or cleared. Thyroxine is the reservoir for triiodothyronine and occurs as thyroglobulin in the colloid state and as protein-bound iodine in the serum. Thyroxine is only slowly absorbed into the cells or converted to triiodothyronine. Thus triiodothyronine acts more rapidly than thyroxine and its action lasts for a much shorter time. *Peter C. Williams*

1382. **Localised Pretibial Myxoedema Treated with Cortisone**

R. S. M. D. Inch and C. F. Rolland. *Lancet* [*Lancet*] **2**, 1239–1241, Dec. 12, 1953. 7 figs., 7 refs.

Three cases of pretibial myxoedema with exophthalmic ophthalmoplegia are reported from the Royal Infirmary, Edinburgh. Treatment for thyrotoxicosis had previously been given to 2 of the patients, both of whom had clubbing of the fingers. The third patient had myxoedema but no previous history of thyrotoxicosis. Cortisone was given systemically or by injection into the site of the pretibial myxoedema. Combined systemic and local treatment was followed by a definite but temporary improvement in the skin condition; local treatment alone, however, was much less effective. Local injection of hyaluronidase, with or without cortisone, proved of little value. The injection of cortisone into the retro-ocular tissues of 2 patients had no effect on the exophthalmic ophthalmoplegia. *A. C. Crooke*

1383. **Two Cases of Myxoedema Attributed to Iodide Administration**

M. E. Morgans and W. R. Trotter. *Lancet* [*Lancet*] **2**, 1335–1337, Dec. 26, 1953. 4 figs., 7 refs.

The authors describe 2 cases of myxoedema which were shown to be due to the administration of iodide. A man of 66 and a housewife of 45 were admitted to London hospitals with obvious signs of myxoedema. The man on admission had a pale, puffy face, dry, cold skin, slurred speech, and an impalpable thyroid gland. The basal metabolic rate (B.M.R.) 5 days after admission was −15% and the plasma cholesterol level 370 mg. per 100 ml. The signs of myxoedema gradually disappeared without treatment. Four days after admission the neck: thigh ratio 2 hours after administration of a dose of radioactive iodine was 6·5, and at 24 hours was still 6·0 (normal ratio between 1 and 10). Six days later, however, the ratio was 46·3 and the urine passed during the 24 hours contained only 5% of the dose. The neck counts during the succeeding days fell rapidly, at a rate of about 11% per day. A sample of serum taken 24 hours after the administration of the radioactive iodine contained 0·7% of the dose per litre, of which 90% was protein-bound. Thereafter the serum radioactivity increased rapidly to a peak value of 2·9% per litre. A third test with radioactive iodine 31 days after admission gave a neck:thigh ratio of 21·7, and a fourth test at 76 days gave a normal ratio of 4·4. The agent which had been suppressing activity of the thyroid gland before admission appeared to be potassium iodide contained in a remedy for rheumatism which the patient had been taking for many years, the dose of iodide amounting to 180 mg. per day.

The female patient, in whom the physical signs were very similar, had been taking 7½ gr. (0·5 g.) of sodium iodide every 4 hours for about 4 years as a constituent of a remedy for asthma. On admission the B.M.R. was −21% and the plasma cholesterol level 300 mg. per 100 ml. The patient's condition improved without treatment, the plasma cholesterol level falling to 150 mg. Tests with radioactive iodine followed a similar course to those in the first case. There was a very small uptake of iodine at 2 and 24 hours on the day following withdrawal of the iodide, but 9 days later the figures were in the thyrotoxic range and did not fall to normal until the 25th day.

The authors suggest that these studies show that the activity of the thyroid gland had been depressed by the administration of iodide and that it could concentrate iodine but not manufacture the hormone. This was followed by a period of release, during which time iodine was passing through the gland and emerging in the blood in a protein-bound form at a rate commonly found in thyrotoxicosis. A few weeks after stopping the supplies of iodide the uptake of radioactive iodine returned to normal. *Norval Taylor*

1384. **Prolonged Treatment of Patients with Hyperthyroidism.** (Langtidsbehandling af patienter med hyperthyreose)

J. Piper and J. Rosen. *Ugeskrift for Læger* [*Ugeskr. Læg.*] **115**, 1820–1824, Dec. 3, 1953. 4 refs.

Prolonged treatment of hyperthyroidism with methylthiouracil, propylthiouracil, methyl mercapto-imidazole, or thiouracil was carried out in 119 cases of hyperthyroidism during an 8-year period at the Frederiksborg County Central Hospital, Denmark. Treatment was incomplete in 28 cases owing to death from other causes (6), size or type of gland (9), poor cooperation by the patient (6), or toxic effects of the drug (7). Of the remaining 91 patients, 49 (41%) were euthyroid at least 6 months after completing the course of treatment, the mean duration of which was nearly 3 years; 28 are still being treated; and the remaining 14 have either just completed treatment or have been referred to the surgeons

for thyroidectomy. Of the 63 patients who have completed the course of treatment, 22 have relapsed (35%). Toxic effects were seen in 24 of the 119 patients, and there were 2 deaths from this cause. *B. Nordin*

1385. **The Treatment of Hyperthyroidism during Pregnancy.** (Behandling af hyperthyreose under graviditet) J. PIPER and J. ROSEN. *Ugeskrift for Læger* [*Ugeskr. Læg.*] **115**, 1824–1830, Dec. 3, 1953. Bibliography.

At the Frederiksborg County Central Hospital, Denmark, 13 women with thyrotoxicosis were treated with antithyroid drugs during 18 pregnancies. Treatment was stopped 2 to 3 months before the expected date of delivery to reduce the risk of injury to the foetus. No fewer than 11 of the mothers relapsed after one course of treatment, but 3 of these responded to further therapy, so that altogether 5 became definitively euthyroid. Of the remainder, 5 are still being treated and 3 have undergone thyroidectomy. Among 16 of the 18 pregnancies, there were 4 miscarriages and one stillbirth. The other 11 went to term and yielded normal babies without goitre; one child is thought to be mentally defective, but there is reason to suppose that this is an inherited trait. *B. Nordin*

1386. **Clinical Trial of Methimazole in Treatment of Thyrotoxicosis**
L. A. G. DAVIDSON. *British Medical Journal* [*Brit. med. J.*] **2**, 1300–1303, Dec. 12, 1953. 1 fig., 36 refs.

Since January, 1950, the author has treated 44 cases of thyrotoxicosis with methimazole. A dose of 15 mg. per day was given until the patient was considered to be euthyroid (15 to 142 days, average 56 days). In all who completed the course a complete remission of symptoms was obtained; 2 patients died from other causes, but the remainder have returned to their normal work. Of these, 18 have ceased treatment, of whom 12 are known to be cured; 8 patients relapsed, 5 because treatment was stopped too soon, and these have been brought under control with further treatment; the remaining patients are still under treatment. Mild toxic reactions were noted in only 2 cases. The drug was found to be more rapidly efficacious and to result in fewer failures than any other antithyroid drug. It was less toxic than methylthiouracil, but slightly more toxic than propylthiouracil. *F. W. Chattaway*

1387. **Treatment of Simple Goiter with Thyroid**
M. A. GREER and E. B. ASTWOOD. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **13**, 1312–1331, Nov., 1953. 47 refs.

During the decade 1895–1905 thyroid extract was extensively given in the treatment of simple goitre with good results, but for unexplained reasons it then lost favour and the literature since that time contains few references to its use. In the 5-year period 1945–50 the present authors treated 50 cases of simple, non-toxic goitre with thyroxine. The usual dosage was 2 to 3 gr. (0·13 to 0·2 g.) of dried thyroid (*U.S.P.*) daily, but the range of dosage was ½ to 6 gr. (32 mg. to 0·4 g.) a day. Treatment was continued until the goitre had disappeared or (usually with increased dosage) until no further decrease in size of the gland seemed likely. Remission usually occurred within 3 to 6 months.

There was complete regression of the thyroid enlargement in 20 of the patients and partial regression in 18; in a control series of 40 cases in which no thyroid treatment was given the figures were 5 and 1 respectively. In cases of nodular goitre, single or multiple, complete regression, partial regression, and no change were noted with equal frequency. The drug was without effect in only 3 of the 23 patients with diffuse goitre. There was little correlation between results and the age and sex of the patient and the size and duration of the goitre. Only 2 patients had a recurrence [but it should be noted that some of the patients had been observed for less than one year after treatment ceased].

It is suggested that the goitres were sporadic rather than endemic, and that they were due not to iodine deficiency, but to some defect of thyroxine synthesis in the thyroid gland. The administered thyroid suppressed pituitary thyrotrophin secretion and allowed the goitre to regress. The period of thyroid rest seemed to correct the original deficiency. *Peter C. Williams*

1388. **Histologic Lesions in the Thyroid Glands of Patients Receiving Radioiodine for Hyperthyroidism**
M. E. DAILEY, S. LINDSAY, and E. R. MILLER. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **13**, 1513–1529, Dec., 1953. 19 figs., 21 refs.

In this paper from the University of California School of Medicine, San Francisco, the authors describe the histology of lesions observed in the thyroid glands of 21 patients given therapeutic doses and 2 patients given test doses of radioactive iodine (^{131}I) for hyperthyroidism associated with hyperplastic or nodular glands; 14 of these patients had been previously treated with iodine or thiouracil, but not within one month of the treatment with ^{131}I. In 21 cases thyroid tissue became available for study after operation for removal of thyroid nodules or because medical treatment was not effective soon enough; all these patients were euthyroid at the time of operation, which was performed 10 to 560 days after the administration of ^{131}I. From 2 patients who died of other causes while still hyperthyroid the material was obtained at necropsy. Total doses of ^{131}I ranged from 0·5 to 24 mc.

The glands were classified in 6 groups on the basis of the histological appearances in the removed tissue. Those in Group 1 (6 cases given 0·5 to 11 mc. 12 to 416 days beforehand) were hyperplastic, with occasional nuclear pleomorphism and interlobular fibrosis. Glands in Group 2 (4 cases given 13 to 18 mc. 159 to 485 days beforehand) showed considerable follicular atrophy; the degenerative changes in the nodules were similar to those in non-irradiated nodular goitres. Glands in Groups 3, 4, and 5 (10 cases given 0·5 to 8 mc. 23 to 96 days beforehand) showed varying degrees of thyroiditis, with syncytial or giant-cell proliferation within degenerating follicles and general lymphocytic infiltration; the appearances in 9 of these glands were exactly or closely similar to those of Hashimoto's disease. Glands in

Group 6 (3 cases given 16 to 23 mc. 231 to 558 days previously) showed lesions usually regarded as characteristic of the late effects of irradiation, namely, diffuse follicular and epithelial atrophy and perilobular and interlobular fibrosis.

When the condition of the glands was correlated with the dosage of ^{131}I and the time elapsing since treatment, those in Groups 2 and 6 were all seen to be in the high-dosage, long-period range, and the changes in these glands must therefore be attributed to the late effects of irradiation. Four of the atrophic glands contained small nodules which were shown by autoradiography to be capable of concentrating iodine; these nodules were probably signs of compensatory regeneration. There was no indication of vascular disease in any of the glands, probably owing to the small doses of ^{131}I employed. Nuclear pleomorphism and hyperchromatism were no commoner than in untreated hyperplastic glands. It is noted that the high incidence of Hashimoto thyroiditis (39%) contrasts with the low incidence (3%) in 2,044 cases of Graves's disease which came to operation without irradiation. The difference is obviously significant; it must be attributed to the effect of treatment with ^{131}I, and is apparently an early effect of low doses. It is concluded that the effect of irradiation with ^{131}I differs in normal and hyperplastic thyroid glands.

Peter C. Williams

1389. **Early Effects of Radioiodine on Human Thyroid Function**

N. B. MYANT. *Clinical Science* [*Clin. Sci.*] **12**, 235–245, Aug., 1953. 6 figs., 11 refs.

An investigation was carried out at University College Hospital, London, to determine the minimum dose of ^{131}I which would affect thyroid function. Initially a dose of 100 μc. of ^{131}I was given to 4 thyrotoxic patients, and then, at approximately weekly intervals, this was increased until doses of 1 to 2 mc. were reached. At the time of each injection the 24-hour uptake of ^{131}I and the secondary rise in plasma radioactivity were determined, the results being used to assess the effect of the previous doses on the function of the thyroid.

After 3 to 5 weeks a reduction in thyroid uptake and in plasma radioactivity was noted. In one patient the reduction in the plasma radioactivity occurred before the thyroid uptake was affected. The total radiation dosage at which depression of thyroid function could just be detected varied from 500 to 10,300 roentgen equivalents. The initial depression of thyroid function appeared, however, to be reversible, further treatment with ^{131}I being required before clinical remission was obtained.

G. Ansell

1390. **The Use of Radioactive Iodine in the Detection of Thyroid Dysfunction**

W. W. DRUMMY. *New England Journal of Medicine* [*New Engl. J. Med.*] **249**, 970–973, Dec. 10, 1953. 3 figs., 13 refs.

A study was made of the routine diagnostic use of the 24-hour accumulation of radioiodine by the thyroid gland as performed in 2,000 persons over the course of three and a half years. Five hundred and ninety-three patients were selected for analysis on the basis of a clear-cut clinical diagnosis.

The values encountered in 221 euthyroid patients, excluding those with goiter and those who had received iodine, thyroid or antithyroid medication, ranged from 11% to 59% of the administered dose. Since 93% of these euthyroid patients had values between 15 and 50%, the test provided good discrimination between normal thyroid function and both myxedema, in which no values greater than 15% were found in 30 patients, and thyrotoxicosis, in which 96% of the values in 70 patients were greater than 50%.

Increased avidity for iodine was noted in 11 of 41 cases of nontoxic diffuse goiter, whereas 15 of 16 cases of nodular goiter were normal in this regard. Low or normal values were observed in hypopituitarism. High values were also seen for one to 6 weeks after cessation of antithyroid medication in euthyroid persons. Erroneously low values were noted after medication with thyroid or with iodine or after the use of iodine-containing radiopaque mediums.—[Author's summary.]

ADRENAL GLANDS

1391. **The 17-Hydroxycorticosterone Content of Human Ascitic Fluid**

C. L. COPE and B. HURLOCK. *British Medical Journal* [*Brit. med. J.*] **2**, 753–755, Oct. 3, 1953. 1 fig., 19 refs.

The difficulty experienced in estimating the small quantities of biologically active steroids present in the peripheral blood prompted the authors to study the steroid content of human ascitic fluid, this being obtainable in larger quantities. Samples of 3 to 7 litres were obtained from "suitable patients", extracted with chloroform, and the extract then taken up successively in acetone (with magnesium chloride) and ethanol, redissolved in chloroform, and evaporated to dryness by a stream of nitrogen.

Extracts equivalent to 1,500 ml. of ascitic fluid were dissolved in propylene glycol and injected subcutaneously into adrenalectomized mice and the fall in eosinophil count determined after 4 and 6 hours, the greater fall being regarded as the significant value. The activity of the fluid was expressed in terms of the equivalent cortisone content, a calibration curve having been prepared by injecting cortisone acetate in various doses into adrenalectomized mice under identical conditions.

Of the 10 samples of ascitic fluid examined in this way by the authors, 5 showed activity equivalent to more than 1·5 μg. of cortisone per 100 ml. Three others gave equivocal results, the activity of samples removed from the same patient at different times varying, while the remaining 2 samples showed no activity at all. Equivalent activity did not exceed 5 μg. per 100 ml. in any sample. Analysis of 4 of the extracts demonstrated the presence of a substance behaving like 17-hydroxycorticosterone, as shown by: (1) its rate of flow on paper chromatography; (2) its ability to reduce the blue tetrazolium reagent; and (3) its absorption of ultraviolet

light at 240 mμ. It was possible to estimate the quantity of 17-hydroxycorticosterone chemically in one extract. Cortisone was detected as a faint trace in only one of the extracts.

The authors tentatively suggest that the hormone content of ascitic fluid may be indicative of the content of extracellular fluid in general, and that their inability to demonstrate any hormonal activity in two of the samples may indicate that under some conditions adrenal cortical hormone diffuses with difficulty from the blood into the extracellular fluid. This might possibly explain the response of the tissues and joints in rheumatoid arthritis to cortisone or 17-hydroxycorticosterone therapy, although adrenal cortical function appears to be normal in this disease. *Robert de Mowbray*

1392. **Effect of Ingested Protein and Tyrosine on Circulating Eosinophils**

I. VARTIAINEN and J. APAJALAHTI. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **13**, 1502–1506, Dec., 1953. 4 figs., 13 refs.

In order to test the assertion of Abelin that the ingestion of protein stimulates the sympathetic nervous system and so produces functional changes, including depression of the leucocyte count, similar to those caused by adrenaline or ACTH, 24 healthy young adult men and women at the University of Helsinki were given gelatin or casein suspended in water, and the changes in the eosinophil cell count were measured after 1, 2, 4, and 6 hours. The dose of each protein was 0·5 g. per kg. body weight.

Gelatin had no effect, but casein caused a fall of 33% in the count by the 4th hour. A similar fall was produced by tyrosine in a dose of 0·3 g. per kg. body weight, and a greater one (43%) with double the dose. The effects thus closely resembled those produced by adrenaline or ACTH. The authors suggest that gelatin may be inactive because of its relative lack of essential amino-acids such as tyrosine and phenylalanine, which constitute a high proportion of the amino-acid content of casein. These two amino-acids are probably basic constituents of adrenaline. Tyrosine itself is poorly absorbed from the intestine and may be better absorbed in polypeptide moieties of casein degradation. *Peter C. Williams*

1393. **Cortisone and A.C.T.H. in Treatment of Non-rheumatic Conditions**

G. M. ABER, G. N. CHANDLER, and S. J. HARTFALL. *British Medical Journal* [*Brit. med. J.*] **1**, 1–8, Jan. 2, 1954. 3 figs., 13 refs.

The effect of cortisone and A.C.T.H. in non-rheumatic diseases has been studied in 43 patients.

Fourteen patients with disorders of the blood have been observed. A favourable response occurred in 3 children with acute acquired haemolytic anaemia, and in thrombocytopenic purpura apparent clinical benefit resulted in the 2 patients treated. No effects were produced in aplastic anaemia, though one patient with acute agranulocytosis from thiouracil made a good response. The effect of A.C.T.H. in leukaemia was at best temporary. This small experience suggests that, apart from acquired haemolytic anaemia and some cases of purpura, cortisone and A.C.T.H. have little place in the treatment of blood disorders.

Sixteen patients with disorders of endocrine function have been studied. Of 9 patients with exophthalmic ophthalmoplegia, only 3 responded well, the best results being obtained with A.C.T.H. in those examples of recent onset or rapid progression. Three patients with Simmonds's disease have made a dramatic and sustained improvement on A.C.T.H. Two patients showing the virilizing effects of adrenal hyperplasia have been treated by adrenalectomy and cortisone: in neither did the results obtained appear to justify the risks involved. 17-Ketosteroid excretion was controlled in two pseudohermaphrodites by the use of cortisone.

The beneficial effect of cortisone and A.C.T.H. in asthma has been confirmed. The use of A.C.T.H. by intravenous drip and of cortisone by inhalation usually brought prompt improvement and was an important economy in prescribing. In 2 patients with nephrosis a considerable diuresis attended treatment, and in one of them the remission obtained has lasted more than a year. There is no evidence that A.C.T.H. influences portal hypertension accompanying cirrhosis, though apparent clinical benefit occurred in one patient.—[Authors' summary.]

1394. **Clinical Aspects of Suppression of Adrenal Cortical Function after Use of Cortisone**

R. M. SALASSA, F. R. KEATING, and R. G. SPRAGUE. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **28**, 662–668, Nov. 18, 1953. 8 refs.

Since cortisone can suppress the function of the adrenal cortex, and since this effect may persist for some time after administration of the drug is stopped, there is a danger of acute adrenal insufficiency occurring after the stress of an operation in patients who have previously received cortisone therapy. The exact duration of the suppressive effect after the withdrawal of cortisone is unknown, but on the basis of available evidence the authors suggest that any patient who has received cortisone in significant amounts within 3 to 6 months of an operation should receive prophylactic treatment and that "any patient who has had extensive hypercortisonism within 1 to 1½ years of a proposed operation should, perhaps, be treated as though liable to acute adrenal insufficiency".

From experience gained at the Mayo Clinic in the operative and postoperative care of patients with Addison's disease the authors suggest that prophylactic treatment should consist in the administration of 200 mg. of cortisone intramuscularly 48, 24, and 1 or 2 hours before operation. Oral administration is not recommended. The administration of cortisone should usually be continued for 3 or 4 days postoperatively in reduced dosage. All patients who have received cortisone therapy before operation, whether or not they have been given prophylactic treatment, should be watched carefully during the first 24 hours since this is the danger period. If acute adrenal insufficiency does develop, the authors recommend the intravenous infusion of isotocin

saline or 5% glucose solution combined with the intravenous injection of cortisone or hydrocortisone if suitable preparations are available. Otherwise, large quantities of aqueous adrenal extract should be given both intravenously and intramuscularly, while noradrenaline in doses of 4 mg. can with advantage be added to the saline; although no immediate effect can be expected, 200 mg. of cortisone should be injected intramuscularly or given by mouth if nausea and vomiting are absent.

D. G. Adamson

1395 **Histopathologic Changes in the Adrenal and Anterior Pituitary in Patients Treated with Cortisone: Preliminary Impressions**

W. A. BENNETT. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **28**, 658–662, Nov. 18, 1953. 4 refs.

The author has studied the adrenal glands of 190 patients who died at the Mayo Clinic of various diseases and who had received various doses of cortisone or related hormones over periods of not less than 5 days within the 4½ months before death. In many cases where a total of more than 450 mg. of cortisone had been given the weight of the adrenal glands was less than normal (6 to 8 g.) and deficient in lipids as shown histologically in sections stained with Sudan IV. These changes were, however, reversible, and normal glands were found in most cases where administration of cortisone had been discontinued more than 6 weeks before death. The whole pattern of adrenal changes appeared to be subject to considerable individual variation.

Mention is also made of unpublished studies by Kilby on the anterior lobe of the pituitary in 77 of the same cases. The basophil cells were affected to a greater or less extent in all cases. The earliest change was clumping of the granules, which later disappeared, with hyalinization and vacuolization of the cytoplasm. The severity of these changes could be correlated with the amount of hormone given, the duration of treatment, and the lapse of time between cessation of treatment and death. Corticotrophin produced earlier and more severe changes than did cortisone.

D. G. Adamson

1396. **Relationship between Actions of Adrenocortical Steroids and Adrenomedullary Hormones in the Production of Eosinopenia**

W. L. HENRY, L. OLINER, and E. R. RAMEY. *American Journal of Physiology* [*Amer. J. Physiol.*] **174**, 455–458, Sept., 1953. 1 fig., 11 refs.

In this paper the authors report, from the University and Michael Reese Hospital, Chicago, their findings on the effects of cortisone and adrenaline on the level of circulating eosinophils in intact and adrenalectomized dogs, in one patient whose adrenal glands had been removed, and in another patient with Addison's disease. Cortisone in a dose of 1 to 3 mg. per kg. body weight intramuscularly produced after 4 hours a significant fall in the number of circulating eosinophils in the intact animals, but not in those which had been adrenalectomized. In the latter the injection of 0·3 mg. of adrenaline 4 hours after the cortisone resulted in a significant reduction of eosinophils in a further 2 hours, whereas adrenaline without preceding cortisone caused a slight rise in eosinophil count. Similarly when the patients, who were both being maintained on cortisone, were given 0·3 mg. of adrenaline subcutaneously the eosinophil count fell by over 60% by the end of 4 hours.

The authors cite other work in agreement with these findings and conclude that adrenaline and the C-11 oxysteroids have a synergic action in producing eosinopenia. They also suggest that in the intact animal adrenaline has the effect of increasing the liberation of ACTH (corticotrophin), which may contribute towards the reduction in the number of eosinophils.

G. A. Smart

1397. **Effect of Derivatives and Analogues of Glycyrrhetinic Acid on Salt and Water Metabolism in Addison's Disease.** (Effect van derivaten en analoga van glycerrhetinezuur op de water- and zout- huishouding bij de ziekte van Addison)

J. GROEN, H. E. PELSER, A. F. WILLEBRANDS, W. L. C. VEER, and G. J. M. VAN DER KERK. *Nederlandsch tijdschrift voor geneeskunde* [*Ned. T. Geneesk.*] **97**, 3290–3300, Dec. 19, 1953. 10 figs., 17 refs.

The administration of extract of liquorice in cases of gastric ulcer has been shown by Revers to cause retention of sodium and chloride, increased excretion of calcium, fluid retention, and an increase in venous, arterial, and pulse pressures, indicating a deoxycortone-like effect. An investigation was therefore undertaken at the Wilhelmina Hospital, Amsterdam, to determine the particular chemical structure responsible for this effect in glycyrrhetinic acid, the active principle of liquorice. Various modifications were made in the chemical structure of glycyrrhetinic acid and the action of these derivatives and of certain related substances on water and salt metabolism in cases of Addison's disease was observed.

While it was not possible to discover the structural basis for the deoxycortone-like effect of liquorice derivatives, it was observed that certain changes, such as acetylation of the hydroxyl group or replacement of the carboxyl group by an indol acetate group did not abolish the typical activity, whereas the effect was lost after removal of an 11-keto group or a change in the position of the carboxyl group in the fifth ring.

R. Crawford

1398. **Maintenance Management of Addison's Disease with Injections of " Long-acting " Microcrystalline Esters of Desoxycorticosterone**

S. Z. SORKIN and L. J. SOFFER. *Metabolism* [*Metabolism*] **2**, 404–410, Sept., 1953. 19 refs.

Two microcrystalline esters of deoxycortone acetate, the trimethylacetate (DCTA) and the phenylacetate (DCPA), were tried at the Mount Sinai Hospital, New York, in the maintenance therapy of 10 patients with Addison's disease. All the patients had previously received deoxycortone acetate parenterally. Aqueous suspensions of the esters were injected into the gluteal muscle, the dosage of the ester being 50 to 120 mg., at intervals of 4 to 6 weeks. It was found that to main-

tain the patient for a month or longer approximately 60 to 75 mg. of ester was required for each milligramme of deoxycortone acetate a day. There was no difference between the results obtained with the two esters.

All the patients were maintained in as good health as they had been with daily injections or with implantation of pellets of deoxycortone acetate. The advantages of this method are the reduction in the number of injections and the fact that the treatment can be given to the ambulatory patient. *D. G. Adamson*

1399. **Adrenal Pseudohermaphroditism**

L. R. BROSTER, J. PATTERSON, and B. CAMBER. *British Medical Journal* [*Brit. med. J.*] **2**, 1288–1291, Dec. 12, 1953. 3 figs., 10 refs.

The clinical and general features of 37 cases of adrenal pseudohermaphroditism, studied by the authors over a period of years, are reviewed in this paper from Charing Cross Hospital, London. Clinical improvement followed unilateral adrenalectomy in all cases, being most marked when the operation was performed before puberty. The excretion of 17-ketosteroids, which was high in all cases, decreased after operation, but was not correlated with the degree of clinical improvement. These patients may be divided into two types, α and β, on the basis of the level of excretion of dehydro*iso*androsterone (DHA), the most important of the beta 17-ketosteroids. Patients of Type α show very low excretion of DHA, and those of Type β have a high rate of excretion (up to 25 mg. per day), but the level of DHA excretion is not related to the clinical picture. Treatment of Type-β patients with amounts of cortisone sufficient to lower the 17-ketosteroid output by 50% also lowers the excretion of DHA by the same amount; if, however, enough cortisone is given to reduce 17-ketosteroid excretion to normal values, DHA is almost completely eliminated from the urine, signifying a change from Type β to Type α.

F. W. Chattaway

PANCREAS

1400. **"Lente" Insulin (Insulin Zinc Suspension): Further Studies**

W. OAKLEY. *British Medical Journal* [*Brit. med. J.*] 2, 1021–1023, Nov. 7, 1953. 3 figs., 3 refs.

The author presents a further report from King's College Hospital, London, on the clinical use of "lente" insulin (insulin zinc suspension), one of the three "novo" long-acting insulin preparations introduced by Hallas-Muller *et al.* (*J. Amer. med. Ass.*, 1952, **150**, 1667; *Abstracts of World Medicine*, 1953, **14**, 59). Lente insulin was used in the treatment of 29 in-patients and 14 out-patients with diabetes. In a first group of 11 patients already under treatment the degree of control obtained with lente insulin was studied by means of frequent estimations of urinary and blood sugar levels, and was shown in 8 cases to be better than that obtained with any previous type of insulin. Of a further 10 cases in which the clinical effect alone was studied, the degree of control with lente insulin was considered to be "good" in 5, "fair" in 2, and "poor" in 2, while in one case lente insulin completely failed to control the hyperglycaemia.

Severe and previously untreated diabetes with ketosis was treated in 8 cases with lente insulin, and in 6 the degree of control was classified as "good", though the time taken to bring the condition under control was probably longer than with soluble insulin.

Out-patient control of diabetes with lente insulin proved successful in nearly all the 14 cases studied. The fact that local reaction appeared to be less than with other preparations promises to be a distinct advantage. Hypoglycaemia, which was infrequent, gave rise to typical symptoms and occurred mostly in the late morning and the afternoon. Nocturnal hypoglycaemia did not occur. *J. N. Harris-Jones*

1401. **The New Insulins—Lente, Ultralente, and Semilente**

I. MURRAY and R. B. WILSON. *British Medical Journal* [*Brit. med. J.*] **2**, 1023–1026, Nov. 7, 1953. 3 figs., 5 refs.

At the Victoria Infirmary, Glasgow, a number of diabetic patients requiring large amounts of insulin, but well controlled with various combinations of soluble and protamine zinc insulin, were given one or other of the "novo" insulins [see Abstract 1400] instead, and the degree of control was compared with that previously achieved. "Lente" insulin was used in 28 cases, and the control achieved was as good as, or better than, it had been with the previous insulin or insulin mixture. Only in 2 cases was it worse. In a large number of cases the dose of the new insulin was almost identical with previous needs. The authors used "semilente" and "ultralente" insulins only occasionally and have little comment to make on them. They were, however, impressed by the almost total absence of local allergic reactions when any of the new insulins were used.

Blood sugar estimations were made at various times of the day while the patient was receiving his original insulin regimen and repeated after the change to lente insulin or a mixture of lente and ultralente insulins. Details of these tests in 15 cases are given and show that in at least 11 cases control was clearly better with the new insulins.

The authors conclude from their studies that the introduction of the new insulins for general use would be fully justified, and would render the use of globin and protamine zinc insulins unnecessary.

J. N. Harris-Jones

1402. **The Insulin Zinc Suspensions**

J. D. N. NABARRO and J. M. STOWERS. *British Medical Journal* [*Brit. med. J.*] **2**, 1027–1030, Nov. 7, 1953. 3 figs., 4 refs.

The authors have studied the action of the "novo" insulins [see Abstract 1400] on 22 diabetic patients at University College Hospital, London. The patients were admitted for initial studies and stabilization, and were selected because of their large insulin needs, requiring two injections a day. Diet was controlled, and the effects of insulin assessed by means of 2-hourly blood

sugar estimations. In 12 cases the diabetes was adequately controlled with a single dose of " lente " insulin, and in a further 6 cases with a single injection of a mixture of lente and " ultralente " insulins, the latter being necessary to overcome evening and early-morning hyperglycaemia. The dose of the new insulins was in most cases of the same order as previous insulin requirements. There was a notable absence of local reactions with the new insulins. Attempts to shorten the action of lente insulin by mixing it with soluble insulin were unsuccessful —indeed, since the soluble insulin crystallized out the effect of the mixture was more prolonged.

These observations lead the authors to conclude that the claim that a single injection of novo insulin will control diabetes in something over 90% of cases is justified. They suggest, however, that the ratio of insulin zinc suspension (amorphous) to insulin zinc suspension (crystalline) in lente insulin for use in Great Britain should be changed from 3:7 to 2:8 to allow for the difference in dietary habits. *J. N. Harris-Jones*

1403. The Classification of Various Insulins

F. GERRITZEN. *British Medical Journal* [*Brit. med. J.*] **2**, 1030–1031, Nov. 7, 1953. 4 figs., 4 refs.

The author has previously described (*Brit. med. J.*, 1952, **1**, 249; *Abstracts of World Medicine*, 1952, **12**, 151) a method of comparing various preparations of insulin according to their duration of action. The results of applying this method to 13 different types of insulin appear to show that the preparations studied fall into four main groups, and that within each group they differ very little in characteristics. These groups are made up as follows. (1) Insulins whose action lasts over a period of 8 hours; these include soluble insulin and " altinsulin ", the former causing a slightly sharper initial fall of blood sugar level. (2) Insulins of which the action lasts over 10 hours; they include the N.P.U. insulins, " depot "-insulin, and the insulin zinc suspensions, " zinc-insulin neutrale ", and " semilente " (" novo ") insulin. (3) Insulins effective for 16 hours; they include " di-insulin ", " iso-insulin ", " lente " (" novo ") insulin, and globin insulin. (4) Those active over 18 hours, for example, protamine zinc insulin and " ultralente " (" novo ") insulin.

[Although the author does not actually say so, his results suggest that many of these insulins are redundant.] *J. N. Harris-Jones*

1404. Spontaneous Hyperinsulinism due to Islet-cell Adenoma

K. O. BLACK, J. P. HOSFORD, R. S. CORBETT, and J. W. ALDREN TURNER. *British Medical Journal* [*Brit. med. J.*] **1**, 55–60, Jan. 9, 1954. 36 refs.

The authors describe 3 cases, seen at St. Bartholomew's Hospital, London, of pancreatic islet-cell adenoma in which attacks of spontaneous hypoglycaemia were eliminated by the surgical removal of the tumour.

In the first case, a man aged 27 was admitted to the hospital complaining of fits. His attacks started with blurring of vision, dizziness, and profuse sweating, followed by loss of consciousness. There was no albumin or sugar in the urine. Starvation for 18 hours caused sweating, drowsiness, and coma. The administration of 5 g. of glucose intravenously caused an immediate return of consciousness. Blood sugar levels during the attacks were about 45 to 48 mg. per 100 ml. No tumour was found when the pancreas was first explored, but partial pancreatectomy alleviated the symptoms. These recurred within a few months, however, and at further exploration an islet-cell adenoma was removed from the head of the pancreas.

In the second case a woman of 22, who first had attacks of hypoglycaemia 6 months previously, was admitted to hospital in deep coma, with spastic limbs and extensor plantar responses. The blood sugar level was 55 mg. per 100 ml. Recovery from coma was slow, and on the 3rd day after admission it became apparent that she had a left hemiplegia. This improved gradually and she was discharged, but during the next few months she had further hypoglycaemic attacks and operation was advised. A purple-coloured tumour, 0·75 cm. in diameter, was removed from the head of the pancreas and section confirmed that this was an islet-cell adenoma. The third case presented a somewhat similar history.

In their discussion the authors stress that in all 3 cases the hypoglycaemic attacks were paroxysmal and that in general they occurred with increasing frequency and severity. They recall that Whipple suggested three criteria for the diagnosis of functioning islet-cell tumours: (1) attacks of nervous or gastro-intestinal disturbance occurring in the fasting state; (2) blood sugar level below 50 mg. per 100 ml. during an attack; (3) immediate relief of symptoms on the ingestion of glucose. The two conditions from which organic hyperinsulinism must be differentiated are hepatic hypoglycaemia and functional hypoglycaemia. No difficulty arises with the hypoglycaemia due to severe parenchymal damage of the liver with jaundice, but hypoglycaemia occasionally occurs in minor liver disorders. The differentiation between organic and functional hypoglycaemia may be difficult, but it is important, as the treatment of the former is surgical and of the latter medical; it can in most cases be made on clinical grounds. In the latter the blood sugar level is normal even after prolonged fasting, and attacks do not occur at night, but are confined to daytime, when they occur 2 to 4 hours after food. The clinical course of organic hyperinsulinism is progressive, whereas in functional hypoglycaemia it is not.

When other causes of hyperinsulinism have been excluded and the diagnosis of organic hyperinsulinism has been made, the pancreas should be explored without delay because of the possibility of malignancy, the risk of permanent damage to the central nervous system, and the increasing obesity. In all the 3 cases described the removal of a solitary islet-cell tumour brought complete relief of symptoms. *J. Lister*

1405. Antidiuresis Associated with Administration of Insulin

J. H. MILLER and M. D. BOGDONOFF. *Journal of Applied Physiology* [*J. appl. Physiol.*] **6**, 509-512, Feb., 1954. 4 refs.

The Rheumatic Diseases

ACUTE RHEUMATISM

1406. **The Treatment of Rheumatic Carditis in Children with Hormones and Salicylates.** (Il trattamento ormonico-salicilico della cardite reumatica del bambino)
G. GELLI and G. MENICHINI. *Archivio italiano di pediatria e puericoltura* [*Arch. ital. Pediat.*] **16**, 85–128, 1953. Bibliography.

The combination of salicylates with cortisone or ACTH (corticotrophin) in the treatment of rheumatic fever allows the use of smaller doses of each substance; it seems probable also from experimental evidence that the two drugs enhance one another's action, and that their use together may prevent the development of adrenal atrophy.

At the Paediatric Institute of the University of Pisa 13 children with rheumatic fever or chorea have been treated in this way, 8 during their first attack. Doses of 25 mg. of ACTH or 50 mg. of cortisone were given daily for 3 weeks and the dose was then halved for a further 3 weeks. Simultaneously, 4 to 6 g. of sodium salicylate was administered daily, this dose also being halved later. In addition, penicillin and streptomycin were given during the whole period of treatment, partly because of a belief in the initial infective nature of the disease and partly to combat any increased risk of infection resulting from the hormone therapy. A low-salt diet with added ascorbic acid was given, and the usual measures for the relief of cardiac failure were instituted when necessary.

All the patients improved rapidly, the most striking effects being noted on the extracardiac manifestations of the disease: one patient with chorea, for instance, lost his symptoms altogether within 10 days. No danger was encountered from fluid retention, and 3 patients in heart failure—one seriously ill—all responded satisfactorily. The effect of the combined therapy on the cardiac lesions was much more difficult to assess: although the signs of endocardial involvement did not progress, in only 2 patients did they entirely disappear, and this during their first attack. As might be expected, myocarditis and pericarditis appeared to be more susceptible to treatment than endocarditis, but the electrocardiogram was of little help in assessing improvement because of the changes produced by the electrolyte disturbances accompanying treatment.

The authors conclude that while the course of the disease was much shortened and, although several were extremely ill initially, no patient in this series died, it cannot yet be said that a form of treatment has been found which materially alters the results of cardiac involvement in rheumatic fever. *A. Paton*

See also Cardiovascular System, Abstract 1347.

CHRONIC RHEUMATISM

1407. **Osteoarthritis of the Shoulder.** (L'arthrose de l'épaule)
F. COSTE, F. LAURENT, and Y. CHAOUAT. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **20**, 675–684, Oct., 1953. 15 figs., 7 refs.

As osteoarthritis of the scapulo-humeral joint is relatively uncommon—in two series quoted, only 18 instances were found in 763 cases of painful shoulder—the authors give a short clinical account of the condition. It is found chiefly in elderly subjects, and is usually secondary to a congenital malformation of the humeral head, to an old osteochondritis, or to severe trauma. The clinical features—namely, dull pain in the shoulder, atrophy of the deltoid, and supra- and infraspinatus muscles with restriction of movement—are similar to those observed in the late stages of the more common scapulohumeral periarthritis, in the slowly progressive shoulder stiffness of senile tuberculosis of the joint, in rheumatoid arthritis, and in the arthritis of ankylosing spondylitis.

The differential diagnosis is discussed, and the several varieties of the condition are illustrated by typical radiographs. The treatment recommended is the administration of vitamins, calcium, or compounds of iodine and sulphur; in some cases mud packs and radiotherapy have proved useful. Mobilization of the shoulder is considered to be dangerous [but the reasons for this are not stated]. *Kenneth Stone*

1408. **Radiological Observations on the Sacro-iliac Joint in 100 Cases of Rheumatoid Arthritis.** (Osservazioni radiologiche sulle articolazioni sacroiliache di 100 malati di poliartrite cronica primaria)
A. ROBECCHI and R. CAPRA. *Reumatismo* [*Reumatismo*] **5**, 298–302, Sept.–Oct., 1953. 15 refs.

While it is generally agreed that typical changes in the sacro-iliac joints are found in all but the earliest cases of ankylosing spondylitis, opinions differ as to whether such changes are associated with this disorder alone, some authors alleging that they occur in a certain percentage of cases of rheumatoid arthritis, and that ankylosing spondylitis is not a separate entity but merely a particular manifestation of rheumatoid arthritis.

In the study here reported from the Ospedale Maggiore, Turin, of 71 female and 29 male patients aged from under 20 to 70 years, with rheumatoid arthritis, the pelvis was examined radiologically. In 76 cases the sacro-iliac joint was judged to be normal. In the remaining 24 cases the joint showed various changes, consisting in most cases in marginal sclerosis and a narrowed and indistinct joint space. Exceptionally, the joint margins were irregular and the joint space was interrupted by bony bridges, but none showed complete disappearance

of the joint line. The changes were not related to the duration of the disease, to the number of other joints involved, or to the involvement or not of the hip-joints, but there appeared to be some relationship with involvement of the lumbar spine. In no case did the changes correspond to the typical evolutionary phases of ankylosing spondylitis, the changes in the sacro-iliac joint of most of the patients being unilateral, a finding considered rare in ankylosing spondylitis. Other workers have reported similar changes in the sacro-iliac joints of non-arthritic subjects, particularly women who have had multiple pregnancies; also such changes are not uncommon in elderly subjects, in whom they are due to degeneration.

The authors conclude from their study that the radiological changes observed in the sacro-iliac joint in cases of rheumatoid arthritis are not significant, as they do not vary substantially from those in non-arthritic subjects of the same age and sex, nor do they present the characteristics generally considered typical of ankylosing spondylitis. They maintain, therefore, that the two diseases are distinct entities. *W. D. Nichol*

1409. **Finger Contractures due to Tendon Lesions as a Mode of Presentation of Rheumatoid Arthritis**
B. M. Ansell and E. G. L. Bywaters. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **12**, 283–289, Dec., 1953. 8 figs., 9 refs.

The tendinous lesions of rheumatoid arthritis are not uncommon, but they may be difficult to recognize if they occur before the arthritic changes develop. In this paper from the Juvenile Rheumatism Unit, Taplow, Berks, and the Postgraduate Medical School of London, 3 cases are described in which the tendinous lesions were the presenting sign and were associated with contracture of the fingers.

A girl of 16 developed painless swelling of the hands and feet followed by stiffness of the fingers, without nodule formation. There was no clinical or radiological evidence of arthritis, but the erythrocyte sedimentation rate (E.S.R.) was raised and the differential agglutination titre for sheep erythrocytes was 1:32 (positive). Biopsy examination of a dorsal tendon sheath showed changes consistent with rheumatoid arthritis. Wax baths and exercises brought about an improvement in mobility of the fingers.

A girl of 8 began to have difficulty in straightening the fingers, and rheumatoid arthritis was diagnosed. She had no pain, and when she was seen at the age of 12 the tendons in the palms were thickened, but there was still no joint involvement. Radiographs of the hands showed minimal healed erosions. The differential agglutination titre was 1:2 (negative) and the E.S.R. was normal. Exploration and mobilization of the flexor tendon sheaths of the hands resulted in an improvement. Biopsy examination of tissue removed at operation showed cellular infiltration without necrosis.

A girl of 12 had painful swelling of the ankles and transient pain in the hands, followed by difficulty in straightening the fingers. The palmar tendons were thickened but there was no clinical or radiological evidence of arthritis. The E.S.R. was 20 mm. per hour (Wintrobe) and the agglutination titre was 1:4. Wax baths and exercises were ineffective and nodular thickening appeared in the tendons. Biopsy of tissue from the Achilles tendon was consistent with juvenile rheumatism. The patient was therefore given a prolonged course of ACTH which resulted in marked improvement; although there was some persistent nodular thickening, there was no functional disability.

The authors also describe a case in which rheumatoid arthritis was complicated by the development of nodules in the hands and by stiffness of the fingers; the patient, a young woman, was eventually unable to use her fingers satisfactorily. When the arthritis was thought to be quiescent the flexor tendon sheaths were incised; this was followed by improvement in mobility.

K. C. Robinson

1410. **Investigation of the Synergistic Action of Cortisone and Tetraethylthiuram Disulfide (Antabuse)**
L. L. Wiesel and A. S. Barritt. *Brooklyn Hospital Journal* [*Brooklyn Hosp. J.*] **11**, 121–124, 1953. 9 refs.

It has been shown that cortisone is rapidly inactivated *in vitro* by liver, spleen, and kidney tissue, and that tetraethylthiuram disulphide (disulfiram) inhibits various oxidative liver enzymes. The authors of the present paper decided to investigate the action of disulfiram in 12 patients with rheumatoid arthritis at the Brooklyn Hospital, New York, who were receiving cortisone and sodium *para*-aminobenzoate. All the patients continued to take 37·5 mg. of cortisone daily, but instead of the sodium *para*-aminobenzoate they were given 500 mg. of disulfiram each day. At first the same degree of symptomatic relief was observed on this regimen as on the previous treatment, but after 2 weeks most of the patients became increasingly drowsy. In spite of a reduction in the dosage of disulfiram drowsiness continued, ranging from mild sleepiness and lethargy in the majority to semi-stupor in one patient. Headache occurred in 2 cases, vertigo and syncope in one, and mental confusion in one; administration of disulfiram was therefore discontinued. It is concluded that although disulfiram acts synergistically with cortisone, it is not suitable for general clinical use.

Kathleen M. Lawther

1411. **Hydrocortone and Soft-tissue Lesions**
J. Cyriax and O. Troisier. *British Medical Journal* [*Brit. med. J.*] **2**, 966–968, Oct. 31, 1953. 1 ref.

The authors of this paper advocate the local injection of "hydrocortone" (Kendall's Compound F; 17-hydroxycorticosterone) for the treatment of chronic inflammation of fibrous tissues resulting from trauma. [No case reports are quoted, however, and there are no references to the literature.] The authors have not found it helpful in the treatment of freezing arthritis [*sic*] of the shoulder, and consider that the indications for manipulation in such cases remain unaltered. They report that tennis elbow and other tendinous lesions respond particularly well to local injections of hydrocortone.

W. S. C. Copeman

Neurology and Neurosurgery

1412. **Spinal Pathways Subserving Defaecation and Sensation from the Lower Bowel**
P. W. NATHAN and M. C. SMITH. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Psychiat.*] **16**, 245–256, Nov., 1953. 20 figs., 9 refs.

Changes in voluntary control and reflex coordination of defaecation and in ano-rectal subjective sensations were studied in 38 patients upon whom antero-lateral cordotomy (20 unilateral and 18 bilateral) was performed for intractable pain. In 23 cases, including 3 with unilateral lesions, the spinal cord was examined histologically as soon as possible after death. Fixation was in 20% formol saline, the staining techniques including the Swank–Davenport modification of the Marchi method, the Kulchitsky–Pal method, and the Gros silver method for fibre changes. Stains used for cell preparations included thionin, haematoxylin and eosin, and Mallory's phosphotungstic acid.

It was found that the pathways subserving the function of defaecation run in the antero-lateral columns within a narrow band extending from the periphery of the cord to the lateral horn of the grey matter. They occupy approximately the same situation at all levels of the cord. It is suggested that the fibres in the lateral part of this band are mainly afferent and the more medial ones mainly efferent. The afferent pathways from the rectum may pass along both sides of the cord, although there may be considerable individual variation in this. The levatores ani and the external sphincter are bilaterally supplied from each side of the cord. Certain clinical implications arising from these conclusions are discussed.

The authors state that they have not yet been able to determine whether or not voluntary control of defaecation is mediated through the cortico-spinal tract.

A. S. Breathnach

1413. **Histamine Treatment of Multiple Sclerosis**
J. K. SMITH and W. F. SCHALLER. *California Medicine* [*Calif. Med.*] **79**, 370–375, Nov., 1953. 22 refs.

The authors point out that the use of histamine in disseminated sclerosis is based upon the theoretical assumption that the disease is due either to allergy or to a vascular affection. They doubt the validity of this assumption and also the value of histamine as a means of increasing the cerebral circulation in man.

They then record their experience of administration of histamine intravenously or by iontophoresis in 20 cases of disseminated sclerosis at the Veterans Administration Hospital, Oakland California. A control group of 16 patients received identical general hospital care but no histamine. The form of treatment varied a little, but generally it consisted in intravenous infusion of 250 ml. of normal saline containing 2·75 mg. of histamine acid phosphate 6 times a week for 2 to 3 weeks. This initial course was followed by iontophoresis for 10 to 15 minutes each day for periods varying up to 4 months. Some patients received intravenous infusion of histamine only; in such cases the course was modified to 3 times weekly for as long as 4 months.

The condition of the patient just before admission was classified as " stationary ", " progressive ", or " acutely exacerbated ". At the end of the trial an improvement was noted in the 5 histamine-treated patients and the 7 controls in the stationary group. In 3 out of 7 histamine-treated patients in the progressive group the condition was unchanged, while in the remaining 4 it was worse; 2 of 3 controls in this group were unaffected and one was worse. Of 8 patients in the acutely exacerbated group who were given histamine, 6 improved and 2 were unchanged. All 6 controls in this group improved.

While recognizing the statistical limitations of their series, the authors draw attention [reasonably] to the fact that in spite of histamine treatment new lesions developed in some cases; they suggest that this is enough to cast doubt upon the efficacy of the drug in the treatment of disseminated sclerosis. In cases in which there was a recent exacerbation of the disease the improvement rate was generally high, but this, the authors point out, occurs regardless of the use of histamine therapy.

L. A. Liversedge

1414. **The Relative Susceptibility to Injury of the Medial and Lateral Popliteal Divisions of the Sciatic Nerve**
S. SUNDERLAND. *British Journal of Surgery* [*Brit. J. Surg.*] **41**, 300–302, Nov., 1953. 1 fig., 10 refs.

In the light of recent work on the internal anatomy of nerve trunks, possible explanations for the generally accepted observation that the lateral popliteal division of the sciatic nerve is injured more often and also suffers greater damage than the medial division were examined by the author in an investigation carried out at the University of Melbourne. Among 67 cases of injury of the sciatic nerve and its popliteal divisions the author found 48 in which the lesion was at a level which permitted assessment of the relative vulnerability of the two divisions. The interval between injury and onset of recovery, progress of recovery, and nature of the residual disability in the fields of the two divisions were assessed in each case, from which it appeared that the effect of trauma was approximately the same on both divisions in 16 cases, while it was greater on the medial division in 6 and on the lateral division in 26 of the remainder. These findings are consistent with those of other observers.

In discussing the anatomical basis for the greater vulnerability of the lateral (peroneal) division, the author points out that although it does overlap the medial (tibial) division posteriorly and superficially to a limited extent, in certain cases in his series a missile had passed nearer the medial division, but had caused more damage to the

lateral division. Other workers have emphasized certain differences in the disposition of the blood vessels supplying the two divisions, those of the lateral being less protected than those of the medial, but apart from cases of paralysis due to pressure injury, the present author does not regard this as a likely explanation. On the other hand, examination of cross-sections of the sciatic trunk and its main divisions showed that in most individuals the lateral popliteal division is made up of fewer and larger bundles with less supporting adipose and epineural tissue than the medial division. Moreover, in the thigh the medial division descends vertically from the sciatic notch to the knee with little fixation at its lower end, so that a displacing force can be dissipated over a greater length of nerve, whereas the lateral division, which descends more obliquely in the thigh, is angulated and relatively firmly fixed at the neck of the fibula, so that there is less slack to take up when it undergoes violent displacement and it is thus subject to greater stretching force, the effect of which is enhanced by the relative lack of supporting connective tissue. *John Huston*

BRAIN AND MENINGES

1415. **The Treatment of Pachymeningitis Haemorrhagica Interna (Haematoma of the Dura Mater).** (Beitrag zur Therapie der Pachymeningitis hämorrhagica interna (Hämatoma Durae matris))
F. KOCH. *Archiv für Kinderheilkunde* [*Arch. Kinderheilk.*] **147**, 213–225, 1953. Bibliography.

In this article from the Paediatric Clinic of the Justus-Liebig Hochschule, Giessen, the author stresses first the inadequacy of our knowledge regarding the aetiology, pathogenesis, and treatment of affections of the dura, and instances the conflicting theories regarding the cause of pachymeningitis haemorrhagica interna. He agrees that the treatment of this condition, like that of chronic subdural haematoma, must be actively surgical, since it has been shown that the administration of vitamins, gelatin, and calcium are without effect, and repeated puncture through the fontanelles succeeds in only a few cases. The fluid may be loculated or so far forward under the frontal bone as to be inaccessible, while the rapid growth of the infant brain renders it extremely desirable to deal effectively with any constricting processes in order to avoid irreparable damage to the organ.

It has been proved impracticable to withdraw the membrane through a trephine hole, on account of the extensive vascularization and the risk of causing unavoidable damage to vessels. In order to avoid these dangers, therefore, the author has evolved a technique of open operation by which both the fluid secretion and the dura can be adequately dealt with. As he points out, a similar operation (but carried out in two stages) was described by Ingraham and Matson 10 years ago (*J. Pediat.*, 1944, **24**, 1), but because of the war was unknown in Germany. The author's operation was therefore developed independently. It is performed in one stage; an incision across the vertex from ear to ear and a butterfly-wing shaped resection of the bone on either side of the sagittal plane permit access to both hemispheres and facilitate the removal of the under layer of the dura which forms the sac of the haematoma.

Out of 37 cases of pachymeningitis haemorrhagica seen since the war, the operation was performed in 17. There were 3 operative deaths, a mortality of 17% (Ingraham and Matson's figure in 169 cases was 2·9%), but the deaths of the author's patients occurred early in the series and in cases in which the disease was complicated by other conditions. In his view the operation should not be undertaken in severely debilitated children, or in the presence of other complications. In most cases it should be considered only after more conservative treatment by fontanelle puncture has proved ineffective over a period of 3 to 4 weeks. The results in the 14 surviving children in this series, observed over 2 to 3 years, have been good as regards bodily and mental development. In comparison, of the 20 patients not operated on, 10 have died, 2 suffer from epilepsy, and one from spastic hemiplegia. The remaining 7 patients show no important features, but they have so far been under observation for less than one year.
D. P. McDonald

1416. **Observations on Epileptic Automatism in a Mental Hospital Population**
D. W. LIDDELL. *Journal of Mental Science* [*J. ment. Sci.*] **99**, 732–748, Oct., 1953. 46 refs.

The part played by temporal-lobe dysfunction in mental disorder was studied in a group of epileptic patients at Runwell Hospital, Essex. Of the 1,110 patients in the hospital, 47 (25 men and 22 women) suffered from epilepsy, and these were examined clinically and by electroencephalography.

Automatism was observed in 18 of the patients, 15 of whom had a well-marked aura preceding the fit; in none of these, however, was there an aura of disturbed taste or smell. Encephalography revealed temporal-lobe dysfunction in 23 patients, including the 18 with automatism.

In the author's view patients with temporal-lobe epilepsy tend to gravitate to mental hospitals because of their anti-social behaviour and unpleasant personality changes. *G. S. Crockett*

CEREBRAL VASCULAR DISORDERS

1417. **Is Stellate Ganglion Block of Value in Stroke?**
J. E. RUBEN and R. A. MAYER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **153**, 1002–1004, Nov. 14, 1953. 11 refs.

The results of stellate-ganglion block in 58 cases of cerebral thrombosis or embolism are reported. In 26 out of 43 acute cases (duration of cerebral vascular disorder less than one month), there was improvement almost immediately after the appearance of Horner's syndrome (the sign of a successful block), the improvement in 17 of these being " dramatic ". Improvement was noted in 4 of the 15 chronic cases.

Describing the method the authors state that the block is repeated daily until no further improvement occurs;

they perform it at least three times at 24-hour intervals before deciding that a patient will not benefit from the treatment. They emphasize that stellate-ganglion block must be combined with physiotherapy and good general medical and nursing care.

Four cases are described in detail, in one of which 22 blocks were performed in 4 months. No untoward effects were observed in any of these cases.

G. S. Crockett

1418. **The Indications for and Results of Surgical Treatment for Cerebral Cirsoid and Arterio-venous Aneurysms.** (Indications et résultats du traitement chirurgical des anévrismes cirsoïdes et des anévrismes artério-veineux du cerveau)

D. PETIT-DUTAILLIS and G. GUIOT. *Presse médicale* [*Presse méd.*] **61**, 1719–1722, Dec. 25, 1953. 9 figs., bibliography.

In continuation of their previous paper (*Presse méd.*, 1953, **61**, 901; *Abstracts of World Medicine*, 1954, **15**, 77), the authors now discuss the surgical treatment of cerebral cirsoid and arterio-venous aneurysms. They point out that until recently most neurosurgeons relied mainly on radiotherapy, and Dandy himself did not venture beyond ligation of the larger arteries in the neighbourhood of the aneurysm or of the carotid at a distance—methods which, owing to the richness of the collateral circulation and to the likely aggravation of the cerebral symptoms following ligation, are now regarded as practically useless, if not actually dangerous; the ligation of the afferent and efferent vessels after exposure may leave some of the more important afferent vessels undiscovered, and thus introduce the grave risk of uncontrollable haemorrhage resulting from rupture of the engorged efferent vessels at the moment of ligation, a catastrophe which even preventive clamping of the carotid will not forestall.

The authors consider that irradiation is of very doubtful efficacy in these cases, and at the Hôpital de la Pitié, Paris, they have evolved a technique for ablation of the aneurysm which they have carried out in 14 cases without an operative death, and of which the end-results have been satisfactory. Out of the 14 patients operated on, 8 were able eventually to resume their occupation without appreciable symptoms, while 3 had mild residual aphasia or motor symptoms; in one case symptoms were aggravated by the operation, in one case of arterio-venous aneurysm of the Sylvian fissure there was temporary improvement but the aneurysm recurred 6 months later, while in the last case in the series, in which an arterio-venous aneurysm was complicated by an intracerebral haematoma, the patient progressed favourably for over one year, after which she had a further stroke and died suddenly 14 months after the original operation. These results agree roughly with those of Olivecrona, who reported excellent results in 51% and functional amelioration in 22% of his cases.

The authors stress that for success to be achieved, the greatest care must be taken in the selection of patients. The case for intervention is clear in the presence of cerebral haemorrhage with signs of compression, but then only after careful arteriographic and ventriculographic investigation has revealed the feasibility of removal. The indication is absolute if arteriography shows the presence of an associated haematoma. At operation, transfusion of 1 to 2 litres of blood is often necessary; the recent introduction of controlled hypotension has marked a considerable advance in operative technique, both in regard to the actual loss of blood and the degree of postoperative shock. In cases where ablation proves impracticable the authors join with Olivecrona in favouring a policy of "all or nothing", but add that perhaps in such cases radiotherapy may be worth trying, with a view not so much to causing regression of the tumour as to stabilizing it.

D. P. McDonald

HYDROCEPHALUS

1419. **Observations on the Effect of Induced Hyperglycemia on the Glucose Content of the Cerebrospinal Fluid in Patients with Hydrocephalus**

J. E. SIFONTES, R. D. B. WILLIAMS, E. M. LINCOLN, and H. CLEMONS. *Journal of Pediatrics* [*J. Pediat.*] **43**, 243–252, Sept., 1953. 12 figs., 6 refs.

The diffusion of glucose from the blood into the cerebrospinal fluid (C.S.F.) in hydrocephalus was studied at Bellevue Hospital (New York University). In normal children the intravenous injection of 1 g. of glucose per kg. body weight resulted in an increase in the glucose content of the lumbar, cisternal, and ventricular C.S.F. of more than 30 mg. per 100 ml. In children with hydrocephalus no such increase occurred. The authors believe that this failure is due chiefly to alteration in the blood–C.S.F. barrier for sugar, and that it cannot be explained on the basis of dilution of the incoming sugar with the greater volume of C.S.F. In patients with hydrocephalus associated with spinal block or active meningitis there was a rapid increase in the sugar content of the lumbar and cisternal C.S.F. after intravenous injection, indicating a local alteration in permeability for glucose. It is suggested that the test may be of some value in demonstrating the presence of spinal blockage in cases of tuberculous meningitis.

J. Foley

1420. **Hydrocephalus Associated with Deficiency of Vitamin A**

J. W. MILLEN, D. H. M. WOOLLAM, and G. E. LAMMING. *Lancet* [*Lancet*] **2**, 1234–1236, Dec. 12, 1953. 3 figs., 11 refs.

At the Agricultural Research Council Unit of Animal Reproduction, Cambridge, the effects of vitamin-A deficiency were studied in 16 young rabbits, aged from 2 weeks to 2 months, born to 5 does which had been kept on a carotene-free diet; no vitamin A was given to the young after weaning. Clinically, all 16 rabbits presented signs of lesions of the nervous system, such as paralysis, especially of the hind legs, and retraction of the head. Pathologically, there was enlargement of the calvarium, and coronal sections of the cerebral hemispheres made post mortem revealed gross dilatation of

the lateral and third ventricles, with extreme reduction of the cortex and white matter, to an extent hardly compatible with life. Laminectomy showed that there was herniation of the cerebellum through the foramen magnum, the optic nerves were constricted at the optic foramina, and the cerebral aqueduct was markedly narrowed at the level of the superior colliculus. Colloidal carbon injected into the ventricles, though plentiful in the lateral and third ventricles, did not pass the constriction and was completely absent from the fourth ventricle.

The authors believe that the lesions observed in these vitamin-A-deficient rabbits can be attributed to the hydrocephalus caused by stenosis of the cerebral aqueduct. These findings are discussed in relation to genetic hydrocephalus in animals and in man, and it is considered that the finding of hydrocephalic young in 5 litters from different matings rules out the possibility of a mutation having been responsible for the condition. The authors conclude: "The discovery of vitamin-A deficiency as a cause of hydrocephalus in the progeny throws open an entirely new field for clinical investigation into the pathology of hydrocephalus, and for experimental observations on the physiology of the cerebrospinal fluid."

[This is an important paper which emphasizes again the significance of environmental factors in the production of yet another congenital malformation. Although the number of animals used was small, the method applied was good. Repetition of the experiments with another species is, however, essential since, as the abstracter has pointed out (*Brit. med. J.*, 1951, **1**, 1110), latent tendencies to a congenital trait which may be only rarely manifested under favourable nutritional conditions may easily be precipitated by lack of specific nutrients in the mother during the organogenic period.]

Z. A. Leitner

TUMOURS

1421. **Parietal Tumours.** (Über parietale Tumoren)
H. Hécaen, M. David, P. van Reeth, and J. Clément. *Wiener Zeitschrift für Nervenheilkunde* [*Wien. Z. Nervenheilk.*] **8**, 1–31, 1953. 5 figs., 20 refs.

In this article from the Hôpital Sainte-Anne, Paris, the authors analyse the findings in 50 cases of parietal-lobe tumour, in 45 of which the diagnosis was confirmed at operation or at necropsy. The tumour was a glioma in 26 cases, meningioma in 11, angioma in 5, and metastatic in 2. There was one case of abscess, and one case of tumour of undetermined nature among the 45 examined histologically. The cases were equally distributed between the sexes and the two sides were equally affected.

Headache was a prominent symptom in 36 cases, papilloedema was seen in 23, and vomiting occurred in 8, but as might be expected, disturbance of sensation was the outstanding symptom. This was frequently paroxysmal in nature, paraesthesiae (formication, numbness, "electric" and dead feelings) occurring in one or more limbs, while objective sensory loss of the cortical type was present in 37 cases. Jacksonian fits occurred in 15 cases, in 7 there was contralateral hyperextensibility of muscles, and adversive attacks away from the side of the lesion were seen in a few cases. Vestibular symptoms of latero- or retropulsion occurred in 7 cases, and visual-field defects were recorded in 21 out of the 32 tested. Psychological changes were noted in 20 cases, with hallucination of one or other of the special senses according to the site of the tumour in a few, and a disturbance of perception with regard to the body image in 23 cases. Apraxia for dressing and visuo-spatial disturbances were found to be useful localizing signs, being associated with right-sided lesions, and 3 drawings by patients are reproduced, illustrating their inability to express ideas of space and shape. In a few cases in which the lesion extended deeply, symptoms of Parkinsonism or hyperaesthesia occurred.

The authors divide their cases according to anatomical site—fronto-parietal (5 cases), parietal (15), parieto-temporal (6), parieto-occipital (17), and parieto-temporo-occipital (7)—and list the main symptoms and signs found in each category. The relations between symptomatology and the pathological type of the tumour are also discussed. *G. S. Crockett*

1422. **A Study of Cerebral Tumours with Primarily Mental Symptomatology.** (Studio sui neoplasmi dell'encefalo ed iniziale sintomatologia psichica)
M. Ferraris, M. Zucchi, and M. De Negri. *Sistema nervoso* [*Sistema nerv.*] **5**, 315–341, Sept.–Oct., 1953. 4 figs., bibliography.

The authors have investigated the occurrence of mental disturbances in 130 cases of intracranial tumour, in most of which the clinical diagnosis had been confirmed at the Neurological Clinic of the University of Genoa by means of carotid arteriography or electroencephalography or both, or at operation. Of these patients, 71 (54%) had mental disturbances at some stage of their illness, but the present paper is devoted to a closer study of the 28 cases (21·5%) in which the mental changes appeared before any abnormal physical signs were to be found in the central nervous system. The tumours concerned were of various types, including glioma, haemangioblastoma, meningioma, and multiple metastases. As regards site, frontal and temporal tumours appear to be the most likely to produce early mental symptoms; in this series the latter occurred most frequently, whereas tumours of the brain-stem, posterior fossa, and hypophysis were absent. Raised intracranial pressure was found in 21 out of the 28 cases, but the mental changes had preceded this by an interval ranging from a few weeks to several years (2 cases). The majority of the patients were between 45 and 60, and it would thus appear that mental changes are most often the presenting symptoms in older patients.

As to the nature of the mental symptoms, the authors agree with previous writers that there is no characteristic psychiatric picture which enables a firm diagnosis of cerebral tumour to be made on such grounds alone, but they suggest that suspicion of such a diagnosis should be aroused by a history of change in character and memory or the development of a neurasthenic syndrome in a patient not constitutionally neurotic, or by atypical depressive conditions in older patients. *J. B. Stanton*

Psychiatry

1423. **Suicide in a State Hospital for the Mentally Ill**
S. Levy and R. H. Southcombe. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **117**, 504–514, June, 1953. 13 refs.

It is pointed out that in 1945 the suicide rate among the general population of the United States was 11·2 per 100,000. Of the 14,782 individuals who committed suicide in that year, 2,783 (18·8%) were in general hospitals and 284 (1·9%) were in mental institutions. In the general population the incidence of suicide was highest in the age group 45 to 54 years, the rate falling thereafter with age. The authors then discuss the incidence of suicide at the Eastern State Hospital, Washington, where, since the institution was opened in 1891, there have been 58 suicides out of a total of 15,199 patients admitted, or 38 per 10,000 admissions. The ratio of males to females was 5:1, and the incidence was highest in the age group 45 to 54 years. Ten of the 58 patients committed suicide within one week of admission, and nearly half within the first 3 months; only 10 committed suicide after being in hospital over 5 years.

A diagnosis of schizophrenia was made in 29 of the 58 cases and of affective psychosis in 11. Depressive features were present in the pre-morbid personality of 10 of the schizophrenic patients, but no depression was observed at any time in the remaining 19. All the 11 patients with affective psychosis, 4 with senile psychosis, and 1 with cerebral arteriosclerosis were in an acute phase of depression. Auditory hallucinations apparently compelled 2 epileptics to commit suicide. Of the 5 patients with general paresis, 3 were depressed and 2 had hallucinations. No depression had been observed at any time in the 2 cases of paranoia and one case of psychopathic personality. One patient with Parkinsonism and one with reactive depression were both depressed. Thus 27 of the patients showed no overt depressive feature, and suicide was probably felt to be the only escape from continuous auditory hallucinations.

Comparison of the suicide rates before and after the introduction of shock therapy showed that the crude rates were 42 and 32 per 10,000 admissions respectively. The authors ascribe the slight decrease not to shock therapy, but to the higher average age of the population, to the proportion of schizophrenics (about half), to the long duration of illness in most cases, and to the fact that there was depression in little more than half the cases.

G. de M. Rudolf

1424. **Psychosomatic Aspects of Infertility**
A. H. Marbach and L. H. Schinfeld. *Obstetrics and Gynecology* [*Obstet. Gynec.*] **2**, 433–441, Nov., 1953. 21 refs.

In this paper from the Albert Einstein Medical Center, Philadelphia, the authors record a number of typical case histories of physically normal women who were unable to become pregnant although apparently desirous of doing so, but who conceived after a course of psychotherapy or, in some cases, after the adoption of a child. Some suggestions are made about possible mechanisms of this "psychogenic" infertility, such as spasm of the uterus or tubes consequent upon emotional tension.

[The interest of the paper lies in the fact that it indicates a serious attempt to treat anxious and infertile women by psychotherapy. Apart from reporting a number of successful therapeutic results, however, it contains little in the way of clinical data and a good deal of speculation. It will be useful as a preliminary introduction to an important field which deserves thorough exploration by physical and psychological methods.]

Desmond O'Neill

1425. **The Effect of Direct Suggestion on Pain Sensitivity in Normal Control Subjects and Psychoneurotic Patients**
W. P. Chapman, J. E. Finesinger, and G. Chesley. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **118**, 19–26, July, 1953. 2 figs., 6 refs.

Experiments to determine the effect of direct suggestion on the perception of pain are described in this paper from the Massachusetts General Hospital and Harvard Medical School. The Hardy–Wolff–Goodell heat radiation apparatus was used to provide a measurable painful stimulus, and the effects of verbal suggestion alone and of a placebo reinforced by verbal suggestion were observed on the thresholds of intensity at which (*a*) the heat stimulus was perceived as painful, and (*b*) motor reaction or wincing occurred. The investigation was carried out on 15 females and 1 male (aged 15 to 58 years) under treatment for psychoneurosis and on 15 healthy female students (aged 17 to 34) who served as controls. The method of applying the cutaneous pain stimulus has been described elsewhere (Chapman *et al.*, *J. clin. Invest.*, 1946, **25**, 890); the time of application was kept constant at 3 seconds and the intensity was varied.

Base-line values for the pain-perception and pain-reaction thresholds were established by performing the test on at least two separate days, and were determined immediately before employing each of the two forms of suggestion, the techniques of which are described in detail, the exact words used being given. In the first technique the stimulus was applied both at the pain-perception level just determined and at 10% below that level, accompanied in each case by verbal suggestion that the subject would, and on another occasion that he would not, feel the pain. In the second technique a placebo containing tinctures of capsicum and cudbear and producing a substernal burning sensation lasting 3 or 4 minutes was presented to the subject with the verbal suggestion that it was an analgesic; 5 minutes was allowed to elapse after it had been taken, and pain-perception and pain-reaction thresholds were then determined without further suggestion.

In both patients and controls the mean value of neither threshold was altered significantly after taking the placebo, such change as did occur being within the limits of variation (±4% for pain reaction) found in preliminary tests. Individually, however, 2 of the patients (both with hysteria) showed a marked rise in both thresholds, while one control subject showed a significant rise in both, and another a significant fall in one. With verbal suggestion only, an increase in pain-perception threshold of at least 10% was observed in 3 out of 12 patients and in 3 out of 15 controls, but with one exception this increase occurred in only one of 3 trials. [In neither of the experiments were differences tested for significance, nor are any statistical measures of variability given.]

The authors conclude that, within the experimental conditions described, suggestion had no appreciable effect on the perception of pain, although it is emphasized that different results might have been obtained if the tests had been carried out by the doctors treating the patients, or if other techniques of suggestion had been used. They suggest that the relief of pain by placebos may be due to the modification of indeterminate factors responsible for the pain rather than to an effect on the threshold of pain perception. *J. C. Kenna*

1426. **Use of Electric-convulsive Therapy in Morphine, Meperidine, and Related Alkaloid Addictions.**
F. B. THIGPEN, C. H. THIGPEN, and H. M. CLECKLEY. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat. (Chicago)*] **70,** 452–458, Oct., 1953. 14 refs.

Wider recognition of the value of electric convulsion therapy (E.C.T.) in the treatment of withdrawal symptoms in cases of drug addiction is urged, the authors giving details of approximately a quarter (35) of the cases so treated at the University Hospital, Augusta, Georgia, since 1948. They quote the findings of Kalinowski and Hoch and of Gallineck in support of their views.

In their own experience, all the intense physiological and emotional disorders accompanying drug withdrawal were abolished by E.C.T., the drug being withdrawn in 3 or 4 days instead of the usual 2 weeks. The method had many advantages over treatment by substitution of amidone, which always caused secondary symptoms.

The number of treatments was determined by the subjective rather than the objective symptoms. In severe cases up to 3 or 4 treatments were given during the first 24 hours, with gradual reduction to one treatment on alternate days. Succinylcholine was given as a relaxant; by this means the complications of E.C.T., including skeletal injury and heart stress, were " virtually eliminated ". In the authors' view E.C.T. accompanied by administration of succinylcholine is less likely to precipitate coronary thrombosis or to lower resistance to infection than are the physiological stresses of gradual withdrawal.

The majority of the 35 patients were morphine or pethidine addicts, but a few cases of codeine, marijuana, dihydromorphinone, or mixed addiction were included in the series. The number of shocks varied from 6 to 19, and the stay in hospital from 6 to 31 days.

[The rationale of E.C.T. and its effect on withdrawal symptoms are well described, but a comparative statistical study with other methods of treatment has yet to be undertaken.] *Richard de Alarcón*

1427. **Electroconvulsive and Insulin Coma Therapy in the Presence of Active Pulmonary Tuberculosis**
L. WEINSTEIN. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **118,** 36–50, July, 1953. 14 figs., 18 refs.

The author discusses the question of the desirability of giving active treatment for mental disease in the presence of pulmonary tuberculosis, and quotes a number of cases from the literature and 33 from his own experience at the Veterans Administration Hospital, Marion, Indiana, as evidence that shock treatment can be given without danger and with good results in many such cases.

A proper evaluation of each case is necessary, but the author believes that ultraconservatism is no longer justifiable. Active treatment of the psychiatric condition should be carried out on all young patients whose prognosis will suffer if it is not given early, quite apart from those patients in whom acute exhaustion or feeding problems make such therapy imperative. Moreover, successful treatment of the mental condition often makes treatment of the tuberculosis easier and more effective. Full details are given of 7 of the author's cases.
J. B. Stanton

1428. **Experience with Reiter Type of Electric Coma at the Boston Psychopathic Hospital**
D. LANDAU and W. L. HOLT. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **118,** 66–71, July, 1953. 4 refs.

The authors describe the treatment with " electric coma " of 20 patients with schizophrenia, all of whom had failed to respond previously to electric convulsion therapy. Coma was induced by the continuous administration of brief direct-current impulses of highly variable intensity (Reiter type), each patient receiving 7 to 30 treatments of approximately 7 minutes' duration at intervals of 2 days. The depth of coma can be controlled by varying the strength of the current after the initial major convulsion and by altering the site of the electrodes, transfer of these from the frontal to the temporal region deepening the coma and vice versa. The patient usually awakes promptly on cessation of the current and is able to eat a meal within 10 minutes. On the basis of their experience the authors consider this treatment to be relatively safe.

Of the 20 patients treated, 5 lost their psychotic symptoms and were able to make a good social adjustment; 10 were less markedly improved, but were well enough to be discharged from hospital; the remaining 5 were unimproved or relapsed after initial improvement. The authors conclude that electric coma is of definite value in the treatment of schizophrenia and has certain administrative and economic advantages over deep insulin coma, but that it does not replace the latter.
J. B. Stanton

Dermatology

1429. **Studies of Sweating. VI. On the Urticariogenic Properties of Human Sweat**
M. B. SULZBERGER, F. HERRMANN, A. BOROTA, and M. B. STRAUSS. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **21**, 293–303, Nov., 1953. 12 refs.

In experiments carried out at New York University Hospital on healthy subjects aged 6 to 54 years, specimens of sweat obtained by exposure of the subject to dry heat proved to be " irregularly but distinctly " urticariogenic on intracutaneous injection into the donor's own skin or the skin of another subject. The urticariogenic effects of sweat in general tended to be more pronounced in some individuals than in others, and was particularly marked in persons with atopic allergy. Sweat collected after a donor's exposure to an inhaled or ingested allergen could not be proved to contain the allergen in question, but nevertheless was more urticariogenic for atopic individuals than ordinary sweat, and the reaction was possibly more pronounced when the recipient was skin-sensitive to the particular allergen.

The authors conclude that these findings support the thesis that autogenous sweat which is forced into the tissues owing to obstruction of the sweat ducts may produce discomfort, itching, and the development of weals, and may thus cause, maintain, or aggravate various dermatoses. *E. W. Prosser Thomas*

1430. **The Use of Silicones to Protect the Skin**
G. MORROW. *California Medicine* [*Calif. Med.*] **80**, 21-22, Jan., 1954. 6 refs.

1431. **Isoniazid (Nydrazid) in Treatment of Cutaneous Diseases**
F. E. CORMIA, M. J. COSTELLO, L. P. BARKER, C. T. NELSON, E. W. WILSON, and J. A. CRAMER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **68**, 536–544, Nov., 1953. 4 figs., 8 refs.

Isoniazid was used by the authors at a number of New York hospitals in the treatment of a variety of skin conditions, a daily dose ranging from 0·2 to 1·2 g. being given for periods of 46 to 186 days. In 7 cases of lupus vulgaris the response to treatment is stated to have been " uniformly good " and there was no evidence that improvement was any more rapid with a dose of 1·2 g. daily than with 0·2 g. daily. Two patients with scrofuloderma were completely cured, but the response to treatment of 11 patients with erythema induratum was poor; 7 of these patients were in the fifth decade of life [but the ages of the others are not stated]. In 3 cases of lepromatous and one of an indeterminate type of leprosy the response was good. No benefit was noted in 4 cases of sarcoid, 3 of dermatitis herpetiformis, and 7 of chronic discoid lupus erythematosus. [The patients do not appear to have been followed up after treatment.]
S. T. Anning

1432. **Isoniazid Therapy of Chronic Dermatoses**
L. C. GOLDBERG and C. R. SIMON. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **68**, 556–565, Nov., 1953. 7 figs., 3 refs.

At the Cincinnati General Hospital (University of Cincinnati) 3 patients aged 27 to 37 years diagnosed as suffering from the Bazin type of erythema induratum were treated with isoniazid in a dosage of 200 to 300 mg. daily for periods of 4 to 9 months. All the active lesions disappeared, but there was immediate relapse on stopping treatment in one patient. [In all 3 cases the treatment was given during the summer months, when spontaneous remissions normally occur.]

Three patients with lupus miliaris disseminatus faciei were also treated with isoniazid with " excellent " results in 2 cases, and 2 patients with tuberculides improved under similar treatment. One patient with a diagnosis of sarcoidosis of the skin and of the lungs was given 100 to 200 mg. of isoniazid daily for 2 months, together with *x* rays to some of the lesions; all the lesions, including those not irradiated, disappeared and no new ones have appeared. [No details of histological or radiological findings in this case are given, and the Mantoux reaction is not recorded. No radiograph of the chest was taken after treatment.] Several patients with chronic discoid and acute disseminated lupus erythematosus did not benefit from treatment with isoniazid.

[There appears to have been no follow-up of these patients.] *S. T. Anning*

See also Pathology, Abstract 1247.

1433. **Induced Fluorescence in the Eczemas.** (La fluorescence provoquée des eczémas)
P. TÉMIME. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph. (Paris)*] **80**, 477–489, Sept.–Oct., 1953. 13 refs.

The author reports that the intravenous injection of fluorescein causes changes in fluorescence in the lesions of eczema which can be observed under ultraviolet light. The variations noted in different types of eczema are tabulated. The same change can be observed in the lesions of experimental eczema and allergy tests, and it is suggested that this might be useful in interpreting doubtful test results. *James Marshall*

1434. **Treatment of Eczema with Cortisone Ointment**
H. VOLLMER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **68**, 525–529, Nov., 1953. 15 refs.

Thirty-five children with atopic dermatitis were treated with cortisone ointments containing between 3 and 25 mg. of cortisone per gram of various ointment bases. Results from 68 treatment periods of at least one week's duration were observed. Eczema was slightly improved in 31

(45·6%), was unimproved in 34 (50·0%), and became worse in 3 (4·4%) instances. Relapses followed improvement in almost all cases after cessation of treatment.

Eosinophile responses to 21 treatments with topically applied cortisone in 15 patients indicated little if any absorption of cortisone into the circulation. It is concluded that local absorption was insufficient, too, in the majority of cases. With the cortisone ointments used, an effective concentration of cortisone was probably not reached in the affected skin layers.

The therapeutic effect of cortisone ointment in eczema does not exceed the results obtainable with conventional dermatologic treatment.—[Author's summary.]

1435. **The Relation between the Effect of Vitamin D_2 and Cholesterol Metabolism in Chronic Eczema.** (Beziehungen zwischen Vitamin D_2-Effekt bei chronischen Ekzemen und Cholesterinstoffwechsel)
W. LUDWIG. *Hautarzt* [*Hautarzt*] **4**, 524, Nov., 1953. 1 fig., 8 refs.

The treatment of 15 cases of resistant or chronic relapsing eczema and neurodermatitis with large doses of vitamin D_2 is reported, 1 to 3 doses of 15 or 20 mg. of " vigantol forte " being given. Clinical results were satisfactory. The serum total cholesterol level was estimated at frequent intervals and was usually found to be increased before treatment, becoming normal during healing of the skin lesions.

It is thought possible that vitamin D_2 influences the passage of cholesterol into the sebaceous glandular apparatus, and animal experiments are described which seem to confirm this hypothesis. When vitamin D_2 in the form of vigantol forte was given to guinea-pigs the serum cholesterol content was found to diminish after 8 hours, remaining at half the normal value for 6 weeks, while at the same time the cholesterol content of the skin rose to nearly double its previous value.

G. W. Csonka

1436. **Erythema Exudativum Multiforme. Its Association with Viral Infections**
C. R. WOMACK and C. C. RANDALL. *American Journal of Medicine* [*Amer. J. Med.*] **15**, 633–644, Nov., 1953. 5 figs., bibliography.

It is first pointed out that there are several syndromes which are now generally regarded as unusual manifestations of erythema multiforme, first described by Hebra in 1866; these include the so-called Stevens–Johnson syndrome, the ectodermosis erosiva pluriorificialis of Rendu, dermatostomatitis as described by Baader, the mucosal respiratory syndrome of Stanyon and Warner, Behcet's syndrome, ulcus vulvae acutum of Lipschutz, and Reiter's syndrome. No single specific cause of erythema multiforme is known; it appears likely that it is an allergic manifestation to a number of different agents.

The authors, after briefly reviewing the literature on the relationship of erythema multiforme to virus infections, report a case seen at the Vanderbilt University Hospital, Nashville, Tennessee, in which the virus of herpes simplex was isolated. The patient, a 19-year-old white woman, developed generalized lesions of herpes simplex infection which at one stage were indistinguishable from the lesions of erythema multiforme. In spite of intensive treatment over a period of 44 days in hospital the patient died from the disease.

In the authors' view sufficient evidence is available to indicate that the virus of herpes simplex is concerned in the pathogenesis of at least some cases of erythema multiforme.

H. R. Vickers

1437. **Pemphigus and Pemphigoid**
A. ROOK and E. WADDINGTON. *British Journal of Dermatology* [*Brit. J. Derm.*] **65**, 425–431, Dec., 1953. 8 refs.

The authors of this paper use the term " pemphigoid " to describe the group of bullous dermatoses which, although histologically like dermatitis herpetiformis, bear more clinical resemblance to pemphigus. In a series of 54 patients with bullous eruptions observed at Addenbrooke's Hospital, Cambridge, and St. Thomas's Hospital, London, for at least a year, 16 cases (including 3 of pemphigus erythematosus) in which the bullae were apparently formed within the epidermis by acantholysis were diagnosed as pemphigus; the remaining 38 cases, in which the bullae were beneath an intact epidermis, were classified as pemphigoid.

From an analysis of these two groups (admittedly small for statistical purposes) the following facts emerge. The sex incidence was approximately equal in patients with pemphigoid, whereas pemphigus occurred three times more often in males than in females. Only one of the 16 patients with pemphigus, but more than half of those with pemphigoid, were over 70 years of age. The lesions in both groups were localized for a variable period after onset, but in all the cases of pemphigus and in 26 of those of pemphigoid they subsequently became generalized to involve the greater part of the body. In pemphigus the most common initial lesion was a localized crusting or mucosal ulceration appearing on the scalp or mucous membranes, whereas in pemphigoid tense, sometimes haemorrhagic bullae, often with urticarial plaques, occurred first on the legs and arms. Mucosal involvement was common and early in pemphigus, but was rarely seen in pemphigoid and then only as a later manifestation.

Excluding the 3 cases of pemphigus erythematosus (Senear–Usher), which are described separately, prognosis was uniformly bad in pemphigus, all 13 cases proving fatal in an average of $8\frac{1}{2}$ months. Pemphigoid, on the other hand, pursued a varied course, with recurrent attacks and remissions; 12 of the 38 patients died after an average duration of the disease of $14\frac{1}{2}$ months. The prognosis of pemphigoid is considered poor in the very old and in cases where there is extensive mucosal involvement. No treatment (ACTH and cortisone were not available at the time) had any beneficial effect in pemphigus, but 32 of the cases of pemphigoid were completely or partially controlled by administration of arsenic, sulphapyridine, acetarsol, or suramin; in 6 cases no form of treatment had any effect.

Benjamin Schwartz

1438. **Studies on Post-Atabrine Dermatitis. II. Permanent Anhidrosis, Anhidrotic Asthenia and Prolonged Dermatitis following Atabrine Dermatitis**
I. L. SCHAMBERG. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **21**, 279–292, Nov., 1953. 6 figs., 31 refs.

In a previous paper (*J. invest. Derm.*, 1951, **17**, 85) the author described prolonged and even permanent disability resulting very occasionally from lichenoid dermatitis due to mepacrine ("atabrine"), and he here reports further observations on this condition. Long-term manifestations include: (1) widespread complete anhidrosis, which makes the patient unfit for any physical exertion in a warm environment; (2) chronic or recurrent lichenoid and eczematous dermatitis; (3) pruritus with minimal or no dermatitis; (4) permanent alopecia; and (5) atrophy of the skin. Patch tests with mepacrine were positive in 2 out of 5 cases, and in one case there was cross-sensitivity to procaine, sulphonamides, and *para*-aminobenzoic acid.

It is suggested that escape of sweat into the cutis as a result of permanent occlusion of the sweat ducts in the presence of functioning sweat glands may be an aetiological factor. *E. W. Prosser Thomas*

1439. **Schaumann's Disease (Sarcoidosis) with Pruriginous Lesions.** (Maladie de Schaumann à forme de prurigo)
J. SCHAUMANN. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph. (Paris)*] **80**, 457–476, Sept.–Oct., 1953. 9 figs.

It was in 1914 that the author described the first case of the disease which is now known by his name. In this paper he recalls that case, describes 6 further personal cases seen since then, and refers to 3 others reported in the literature, a total of 10 cases in which patients with sarcoidosis, with or without skin lesions histologically typical of that condition, presented pruriginous lesions. In 5 of the author's cases there was papular prurigo, one patient had urticarial lesions, and another pruritus only. Histologically, the prurigo papules were seen to consist of intradermal vesicles with varying degrees of dermal lymphocytic infiltration; the typical picture of sarcoidosis was not reproduced. In the author's opinion the prurigo may be attributable to the toxic products of pathological tissue and may well be auto-allergic in nature; the occurrence of the phenomenon seems to add to the evidence in favour of classifying sarcoidosis as a disease of the reticulo-endothelial system. *James Marshall*

TUMOURS

1440. **Cutaneous Melanoma: Ulceration as a Prognostic Sign**
V. N. TOMPKINS. *Cancer* [*Cancer (N.Y.)*] **6**, 1215–1218, Nov., 1953. 8 refs.

Some authors have described cases of cutaneous melanoma in which no correlation was found between the gross and histological findings and the subsequent behaviour of the tumour. The investigation described in this paper from the New York State Department of Health was undertaken to determine whether an objective prognosis could be reached on the basis of available material. A follow-up study of a highly-selected series of 46 cases of primary cutaneous melanoma showed that ulceration, especially in a large growth, was of grave prognostic significance, regardless of the site of origin of the tumour or the sex of the patient. There was some indication that in the absence of ulceration the prognosis was good, but the author is careful to point out that the number of cases was too small for definite conclusions to be drawn. *G. B. Mitchell-Heggs*

1441. **Clinical and Histological Changes in Cutaneous Epitheliomata Treated with Local Infiltrations of Oestrogens.** (Modificationi cliniche e istologiche di epiteliomi cutanei trattati con infiltrazioni locali di estrogeni)
A. AGOSTINI. *Archivio italiano di dermatologia, sifilografia e venereologia* [*Arch. ital. Derm.*] **25**, 397–422, 1952–1953. 16 figs., 31 refs.

The author describes his treatment of cutaneous epitheliomata occurring at sites other than the genital organs by the local infiltration of water-soluble oestrogens. The results are claimed to be good [but the author does not state the compounds used or the dosages required to achieve these results].

A large part of the paper is devoted to a description of histological studies from which it was concluded that, as a result of this treatment, there was definite inhibition and regression of neoplastic tissue, followed by hyperactivity of normal surrounding tissues. *G. Calcutt*

1442. **Electrosurgery for the Treatment of Cutaneous Neoplasms**
A. C. CIPOLLARO. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **34**, 621–626, Oct., 1953.

Electrosurgical currents are adequate, safe and efficient for the treatment of most benign and malignant tumors of the skin. Electrodesiccation is employed far more frequently than electrocutting or electrocoagulation and, therefore, a "spark gap" high frequency apparatus is more desirable than a "tube" machine. For the treatment of most neoplasms local procaine anesthesia is usually employed. The use of the curet is an essential part of the procedure of destroying cutaneous lesions with electrosurgery. Rudimentary rules of surgical procedures and of antisepsis must be employed for successful results. It is seldom necessary to hospitalize patients treated with electrosurgery.

The following tumors especially lend themselves to treatment with electrosurgery: adenoma sebaceum, angioma, cutaneous horn, dermatofibrosarcoma protuberans, epitheliomas, fibroma, fibrosarcoma, granuloma pyogenicum, Kaposi's sarcoma, keloid, keratoses, lipoma, melanoma, myoblastoma, nevi, rhinophyma, verruccae, xanthoma and xeroderma pigmentosum. Some of these tumors may also be treated with other methods. The detailed technic for the treatment of the more important tumors has been outlined.—[Author's summary.]

Paediatrics

1443. **Lactation and Fluid Intake**
R. S. ILLINGWORTH and B. KILPATRICK. *Lancet* [*Lancet*] **2**, 1175–1177, Dec. 5, 1953. 6 refs.

A controlled investigation was made on the relationship of fluid intake to the amount of milk produced by 210 mothers in a maternity unit. 106 mothers were given no instruction about how much fluid they should take, being left to drink what they wanted. The average daily amount of fluid drunk by them was 69·1 oz. [1·96 litres]. 104 mothers were instructed to take at least 6 pints [3·4 litres] of fluid a day; the average daily quantity taken by them was 107·5 oz. [3 litres].

The gain in weight of the babies, the result of test feeds, and the incidence of full breast-feeding were observed, the babies being divided into three birth-weight groups. There was no evidence that the forcing of fluids had any beneficial effect on lactation. On the contrary, there was evidence that more milk was produced by mothers who only drank enough to satisfy their needs.

When the amount of fluid taken by all the mothers was correlated with the test feeds, there was a significant negative correlation coefficient in favour of letting the mothers satisfy their fluid needs without being asked to take more fluid.

The practice of instructing lactating women to drink large quantities of fluid should be abandoned. They should merely take enough to satisfy their own desires.—[Authors' summary.]

NEONATAL DISORDERS

1444. **Resuscitation of the Newborn with Intragastric Oxygen (Akerren's Method)**
H. K. WALLER and D. MORRIS. *Lancet* [*Lancet*] **2**, 951–953, Nov. 7, 1953. 1 fig., 5 refs.

A method of resuscitation of the newborn by intragastric administration of oxygen, as originally described by Åkerrén and Fürstenberg (*J. Obstet. Gynaec. Brit. Emp.*, 1950, **57**, 705; *Abstracts of World Surgery*, 1951, **9**, 212), has been tried at the British Hospital for Mothers and Babies, Woolwich, London. Two rubber catheters are used, size Jacques 3 or 5, depending on the size of the infant. The first catheter is passed and the contents of the stomach are aspirated, the end of this catheter being then placed under water in a gallipot. The second catheter is passed and connected to a supply of oxygen. Oxygen flow through the stomach is indicated by the gas bubbling out of the first catheter.

This technique has been tried in all cases of delayed or unsatisfactory respiration; it has also been used in cases of white asphyxia. With a flow of oxygen not exceeding one litre per minute there was no undue distension of the abdomen. Of 48 consecutive infants so treated, 7 did not respond and died; of the remaining 41, 3 died later. Post-mortem examination revealed severe cerebral damage in 3, and atelectasis and asphyxia in 7. [There were no controls.]

It is suggested that by this method the further depression of the respiratory centre caused by continued anoxia is avoided. An apparatus for use in domiciliary confinement is described.

[Attention has been drawn to the danger of rupture of the stomach with this technique. Ostry (*J. Obstet. Gynaec. Brit. Emp.*, 1951, **58**, 1034) recommends a shortened Miller–Abbott tube for intragastric insufflation in asphyxia neonatorum.] *H. G. Farquhar*

1445. **Treatment of Asphyxia Neonatorum**
J. M. LORD, B. W. POWELL, and H. ROBERTS. *Lancet* [*Lancet*] **2**, 1001–1004, Nov. 14, 1953. 14 refs.

The authors describe the methods used, and analyse the results obtained, in the treatment of asphyxia neonatorum during the 4-year period 1949–52 at the Hammersmith Hospital, London. During this time all such cases have been treated with endotracheal oxygen, and during the last 12 months this has been supplemented, as necessary, with pharyngeal aspiration for babies born by Caesarean section, gastric oxygen for small premature infants (under 4 lb. (1·8 kg.) in weight), and the use of "augmented respiration". The usual routine is as follows.

After aspiration, when there is only moderate asphyxia, a small metal airway is inserted and the baby rocked in an oxygen box; if there is no response in 5 minutes, or immediately in cases of severe asphyxia, an endotracheal tube (No. 00 Magill) is inserted and oxygen supplied at 1·5 litre a minute through the smaller of the two arms of a metal Y-piece connected to the tube. If this does not bring about spontaneous respiration, the open end of the Y-piece is occluded with the finger, for not more than 2 seconds at a time, 12 to 15 times per minute. Experience has shown that if there is any doubt as to the severity of the asphyxia in borderline cases, it is better to give endotracheal oxygen early and omit the preliminary rocking, especially in the case of infants born by Caesarean section.

As small premature infants rarely suffer from complete initial apnoea, oxygen is now given intragastrically rather than endotracheally on the assumption that this will oxygenate the blood sufficiently to enable the respiratory centres to recover and initiate respiration. The oxygen is administered through a 1-mm. polythene tube attached by a 16-gauge needle to the source of oxygen, which is run in at about 0·25 litre a minute, postural drainage and pharyngeal suction being employed at the same time and respiration augmented if necessary.

Out of 7,407 infants born alive during the period under review, 72 were treated by intubation within a few minutes of birth. Of the 45 born at term (most of

them by Caesarean section), 3 died; the asphyxia in all 3 was severe, but even so, scattered areas of aeration were found in both lungs at necropsy. Nine other full-term infants, who for one reason or another were not intubated, died of asphyxia. Of the 27 premature infants who were given oxygen endotracheally, 9 died. Although intubation is regarded as unsatisfactory in any but the largest of premature babies, the authors have hesitated to replace endotracheal entirely by intragastric administration of oxygen, and have therefore no experience of the results of the latter treatment given alone.

They are convinced that in skilled hands these methods should reduce postnatal deaths from uncomplicated asphyxia to a minimum. *Elaine M. Osborne*

1446. **Neonatal Pneumonia.** [In English]
E. K. AHVENAINEN. *Annales medicinae internae Fenniae* [*Ann. Med. intern. Fenn.*] **42**, Suppl. 17, 1–33, 1953. 1 fig., 7 refs.

CLINICAL PAEDIATRICS

1447. **Gastro-enteritis in Infancy**
LONDON COUNTY COUNCIL PUBLIC HEALTH DEPARTMENT. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **7**, 194–204, Oct., 1953. 3 refs.

Some of the aetiological and epidemiological features of infantile gastroenteritis, as revealed by an investigation carried out between July, 1949, and November, 1950, in 9 metropolitan boroughs in the County of London, are discussed. The hospitals in the area voluntarily notified all cases of diarrhoea and vomiting in children under 2 years of age, and the information collected from a questionary and domiciliary visits in respect of 360 children, 220 of whom were admitted to the gastroenteritis unit of one hospital, was analysed.

No seasonal incidence of gastroenteritis was noted. Boys were more frequently affected than girls, the ratio being nearly 2:1. Two peaks in the age incidence were noted in infants admitted from their own homes, at 1 to 2 months and 11 to 12 months, but the incidence in infants between 1 month and 5 months admitted from institutions was steady. Only 22 of the infants were completely breast-fed, and most of these were exposed to "higher-than-average" risks of infection. Bearing in mind the fact that in the general population of the area 31% of the infants were breast-fed at 6 months, the incidence of gastroenteritis was very much higher in bottle-fed than in breast-fed infants. Of the 360 infants, 37 did not have diarrhoea after admission to hospital, but in 71 symptoms were so severe that parenteral therapy had to be given; 15 patients (4·6% of those with diarrhoea) died.

The illegitimacy rate was high, 60 infants being illegitimate (16·2% compared with 9·6% in the general population). The proportion of infants from social Classes IV and V (45·1%) was higher than that in the general population of the area (29%) while the proportion from Classes I and II was abnormally low (5·2%) compared with that in the general population (19·3%). The average size of the household from which patients came was larger than that in the general population, and there was an undue proportion of children (86) from "communally-accommodated families" and residential nurseries. Overcrowding was common; one-third of the families had to share washing-up facilities with another household, while two-thirds shared a water-closet, these figures being double those for the county as a whole.

The standard of cleanliness in about three-fifths of the homes of affected infants was unsatisfactory and methods of preparing milk feeds left much to be desired. In a large proportion of cases other children of the same household had had an attack of gastroenteritis, while 103 of the 360 had a history of poor general health, 67 having previously been admitted to hospital for various reasons.

Other infections, mainly respiratory, were present in one-third of the cases. In almost half there was a recent history of contact with a patient suffering from diarrhoea. Institutional cross-infection was an important factor in the spread of the disease; of interest in this connexion is the number of infants (44) who were admitted from residential nurseries. The presumed causative organism was isolated from the stools of only 27 of the 220 infants admitted to hospital. *J. Lorber*

1448. **Antibiotic and Chemotherapeutic Agents in the Treatment of Infantile Diarrhoea and Vomiting**
MEDICAL RESEARCH COUNCIL, ANTIBIOTICS CLINICAL TRIALS COMMITTEE. *Lancet* [*Lancet*] **2**, 1163–1169, Dec. 5, 1953. 20 refs.

In an investigation of the clinical effects of the oral administration of antibiotic and chemotherapeutic agents, 1,168 cases of infantile diarrhoea (excluding *Salmonella* and *Shigella* infections) occurring over a period of about 2 years at 10 centres in Great Britain were observed. The drugs were given as follows: 154 cases were treated with aureomycin, 415 with chloramphenicol, and 247 with sulphadiazine; there were 352 control subjects some of whom were occasionally given antibiotics when there was no response to routine treatment and the withholding of further therapy could not be justified. The patients were classified within 24 hours of admission into one of six groups based on age and the severity of the disease. Each centre continued to use its own routine method of treatment, but the drugs under trial were given according to an agreed schedule, namely: aureomycin, 75 mg. per lb. (165 mg. per kg.) body weight per day; chloramphenicol, 75 mg. per lb. per day; and sulphadiazine, 125 mg. per lb. (275 mg. per kg.) per day. The drugs were given at intervals of not more than 6 hours for 7 days. Trial drugs were not given to control subjects except in the circumstances already mentioned, but at one centre all severely ill patients were given sulphadiazine and at another penicillin was given as a routine prophylactic in intravenous therapy.

The results in different treatment groups were compared in two stages, each trial being first considered separately, and then the findings in similar treatment groups at different centres brought together. Variations in treatment were also examined. The three groups

finally compared were those comprising aureomycin-treated cases and concurrent controls, chloramphenicol-treated cases and concurrent controls, and chloramphenicol-treated and concurrent sulphadiazine-treated cases. The criteria adopted were the number of deaths in each group, the average duration of diarrhoea after institution of treatment, the average time before clinical recovery was evident, the number of mild cases which became severe, and the number of relapses, that is, diarrhoea recurring within 14 days of apparent clinical recovery.

There was no statistical difference between the aureomycin-treated group and controls, except that among the controls more mild cases became severe. The chloramphenicol-treated patients progressed more favourably than their controls, and the sulphadiazine-treated group fared better than any other. The fatality rate was not thought to be a sound basis of comparison, since the number of deaths in the control group might have been influenced by the occasional use of the trial drugs in severely ill children in that group.

Bacteriological investigations were carried out at five centres particularly to determine the prevalence of *Bacterium coli* O111 and O55, the finding of which has been reported in numerous previous studies of infantile diarrhoea and vomiting. These organisms were equally distributed among the treatment groups in 4 out of the 5 centres, although in one centre (Birmingham) they occurred in higher proportions in the chloramphenicol-treated group for no obvious reason.

[This paper illustrates the difficulties arising in making an evaluation of drugs in these cases.]

J. G. Jamieson

1449. **Hirschsprung's Disease with Associated Intestinal Haemorrhage**

R. E. Horton and B. Laurance. *Lancet* [*Lancet*] **2**, 1288–1290, Dec. 19, 1953. 4 figs., 8 refs.

1450. **Pulmonary Resection in the First Year of Life**

E. S. Crossett and R. R. Shaw. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **97**, 417–424, Oct., 1953. 7 figs., 6 refs.

Advances in anaesthesia, surgical technique, and knowledge of respiratory physiology; have made it possible to perform pulmonary resection in infants with a high degree of safety. In this paper the indications for the operation and the results obtained in 6 cases at Baylor Hospital (University of Texas), Dallas, are described. The authors perform pulmonary resection in cases of (1) balloon cyst, (2) localized hypertrophic emphysema, (3) localized foetal atelectasis, and (4) localized bronchiectasis with symptoms or retarded development. The clinical features and differential diagnosis of these conditions are discussed.

Operation was successful in 3 cases of balloon cyst, 2 infants undergoing lobectomy at the age of 4 months and one local excision of the cyst at the age of 2 months. Resection of the right upper lobe and apical segment of the lower lobe was successfully performed for localized foetal atelectasis in one infant aged 7½ months. Lobectomy was carried out in 2 cases of bronchiectasis associated with cystic pancreatitis in an endeavour to control the pulmonary suppuration. but the infants survived only for 2 months and 8 months respectively.

The authors recommend tracheotomy before and after operation in all cases in which secretion cannot otherwise be adequately controlled. *F. J. Sambrook Gowar*

1451. **Progressive Infantile Emphysema. A Surgical Emergency**

J. L. Ehrenhaft and R. E. Taber. *Surgery* [*Surgery*] **34**, 412–425, Sept., 1953. 10 figs., 15 refs.

The authors draw attention to the syndrome of progressive infantile emphysema, pointing out that if the condition is recognized in time, surgical treatment may save the child's life. The syndrome is due to a rapidly expanding intrapleural lesion, such as a congenital cyst or an area of obstructive emphysema, which causes progressive dyspnoea and cyanosis with atelectasis of the surrounding normal lung and of the other lung, shift of the heart and mediastinum, depression of the diaphragm, and finally death from anoxia. Clinically, the thorax is of the severely emphysematous type with limited costal excursion during respiratory efforts, and intermittent cyanosis, tracheal shift, and unilateral hyperresonance with diminished breath sounds are present. Radiographs show progressive emphysema, mediastinal shift, atelectasis, and herniation of the lung through the anterior mediastinum.

The treatment of localized emphysema is by resection of the involved lung tissue, thus restoring the intrapleural pressure, allowing the expansion of atelectatic lung, and improving the venous return to the heart. The period between intubation of the trachea for anaesthetic purposes and the opening of the pleural space is critically dangerous, as the emphysema progresses rapidly under positive-pressure insufflation of oxygen.

The authors describe 4 cases, 2 in infants of 5 and 4½ months respectively with cystic conditions in the lung, and 2 cases of right middle-lobe emphysema occurring at 14 and 16 days respectively; all were treated successfully by resection, although one infant died one month later with widespread cystic disease. They discuss the possible causes of valvular bronchial obstruction and other aetiological factors, and refer briefly to 3 fatal cases in which over-vigorous resuscitation treatment at birth was probably a major cause of the emphysema.

A. W. Franklin

1452. **Carcinoma of the Thyroid in Childhood and Adolescence**

S. Warren, M. Alvizouri, and B. P. Colcock. *Cancer* [*Cancer* (*N.Y.*)] **6**, 1139–1146, Nov., 1953. 2 figs., 27 refs.

Of 612 patients operated on for carcinoma of the thyroid at the Lahey Clinic, Boston, between 1928 and and 1951, 23 (3·7%) were under 20 years of age. There were 19 females and 4 males, a preponderance of females which is characteristic of the disease in later life. In some of the cases an adenoma which had been present since birth was the site of the carcinoma. No significant

aetiological factors were found; prophylactic irradiation of the thymus was not a causative factor, and none of the parents gave a history of thyroid disease. The duration of symptoms was 3 months to 9 years (average 2 years). Lymph-node metastases were present in 14 of the patients when first seen; in 6 of these "lateral aberrant thyroid" had been diagnosed. The next most frequent site of metastasis was the lung.

The results of treatment, which consisted in radical surgery and deep *x*-ray therapy, confirmed the known fact that carcinoma of the thyroid in childhood is a rather protracted disease which, however, is amenable to treatment in many cases. Because of its relatively benign character the prognosis is favourable.

W. Mestitz

1453. **Congenital Stippling of the Epiphyses or Foetal Epiphysial Chondrodystrophic Calcinosis.** (La maladie congénitale des épiphyses pointillées ou calcinose fœtale épiphysaire chondrodystrophiante)

M. JEUNE, F. LARBRE, R. CARRON, and I. COUETTE. *Archives françaises de pédiatrie* [*Arch. franç. Pédiat.*] **10**, 914–942, 1953. 6 figs., 40 refs.

The authors describe what they believe to be the first case reported in France of foetal epiphysial chondrodystrophic calcinosis. The patient's family was healthy but pregnancy was marked by threatened abortion at the 4th and 7th months. The child, though born at the 8th month, weighed 3,040 g. (6½ lb.). At the 10th day it was seen to be stunted, the stunting affecting the proximal halves of the limbs more than the distal. The terminal joints of both 5th fingers were held flexed and the left thigh could not be extended without causing pain. The skin was hyperkeratotic and desquamating, and appeared to be thickened. The eyebrows were absent, the eyelashes rudimentary, and there was bilateral total cataract. Radiography showed stippling of many of the epiphyses, more marked on the left side. In the left femur the diaphysis and metaphysis were affected, leading to more marked shortening of this bone, and there was fragmentation of the inner half of the metaphysis, resulting in incurvation of the lower end of the bone.

During the first 8 months of life the child's condition was precarious and the stunting became proportionally greater. The disease ran a recurrent febrile course, during which repeated biochemical investigations revealed a hyperchloraemic acidosis with an alkaline urine suggestive of the Lightwood–Albright syndrome. No calcification could be detected radiologically in the kidneys. After the age of 8 months, however, improvement took place in growth, in the skin, and in the radiological appearance, so that at one year the only radiological abnormality was an irregularity of the line of ossification of the lower end of the femur with some curving of the latter, and slight calcification in the left tarsus. The cataract was successfully operated upon.

The authors discuss the symptomatology, pathology, aetiology, prognosis, and radiological findings with reference to this case and 39 others reported in the literature. From this study they conclude that there are two forms of the disease: a major type with a poor prognosis, showing multiple stippling of the epiphyses, evidence of chondrodystrophy with shortening of the limbs usually affecting the proximal halves, and frequently accompanied by cataract and skin abnormalities; and a minor form, in which stippling of the epiphyses can be recognized radiologically, but in which there are no clinical signs. They regard these two types as of common aetiology because of the identical stippling of the epiphyses and because of the existence of intermediate forms, and consider that the primary cause of the disease is the deposition of calcium in the epiphyses, which in turn leads to other bony abnormalities. The disease may be hereditary.

H. G. Farquhar

1454. **Intelligence Levels in Cerebral Palsied Children**

L. B. HOHMAN. *American Journal of Physical Medicine* [*Amer. J. phys. Med.*] **32**, 282–290, Oct., 1953. 6 figs., 2 refs.

In order to determine the incidence of mental retardation among children with cerebral palsy, the case records of the first 600 children referred to the Cerebral Palsy Hospital of the State of North Carolina for examination to determine their eligibility for admission or treatment were analysed. The examination of these children, none of whom was over 16, included both physical and psychological evaluation, the psychometric tests used being the Stanford revision of the Binet–Simon test, the Vineland Social Maturity Scale, the Merrill–Palmer test, and the Cornell–Coxe test. The records of 50 cases in which mental deficiency was the primary problem were discarded, and those of 73 others were found to be incomplete or otherwise unsuitable. Of the 477 children included in the analysis, a satisfactory assessment of intelligence was possible in 269 (56%) and an adequate assessment without detailed accuracy in 165 (34%); in only 43 (9%) was the physical disability such that the tests could not be satisfactorily applied.

The results of the investigation are presented graphically, together with those of Asher and Schonell (*Arch. Dis. Childh.*, 1950, **25**, 360) in England and of Miller and Rosenfeld (*J. Paediat.*, 1952, **41**, 613) in the United States for comparison. The present series is divided by age into 3 groups—7 months to 3 years, 3 to 6 years, and 6 to 16 years—the results in which are very similar, while the over-all results compare closely with those of the other two investigations. In only 16% was the I.Q. above 90 (compared with approximately 80% of the normal population), and in only 3% above 110. At the other end of the scale, in 60% it was below 70, and in 37% it was below 50.

The author suggests that intensive treatment by highly trained personnel should be reserved for the small proportion of children with cerebral palsy, representing one-sixth or less of the total, whose intelligence is normal and whose physical handicaps are not so great as to nullify the effects of such treatment. For the remainder, the aim should be to make the child "capable of self care without attempting the impossible task of making him socially and economically independent".

E. H. Johnson

Public Health

1455. **Poliomyelitis in Hidalgo County, Texas, 1948. Epidemiologic Observations**
R. S. PAFFENBARGER and J. WATT. *American Journal of Hygiene* [*Amer. J. Hyg.*] **58**, 269–287, Nov., 1953. 4 figs., 14 refs.

The occurrence of an outbreak of poliomyelitis in 1948 at the end of a 2-year period of fly control in 9 towns in Hidalgo County, Texas—undertaken primarily to determine its effect on the incidence of diarrhoeal diseases—provided the opportunity to assess the relative importance of man and flies as vectors in the spread of the disease. In Hidalgo County the epidemic started in February, reached its maximum in April, and ended in September, whereas in the neighbouring Cameron and Wallacy Counties, in which control observations were made, it started in April and ended in August or September, with a peak incidence in May in the former county and an even distribution of cases in the latter. The main study dealt with paralytic cases, in all of which information was obtained on possible sources of infection and home environment. Fly control with DDT was maintained during the 8 months of the epidemic in the same 9 towns. The prevalence of flies, as estimated by repeated counts, was always lower in the towns treated with DDT than in the untreated towns. In all towns fly counts were at their lowest in February, the beginning of the epidemic. In the untreated towns the number rose in March, reached a maximum in April to July, fell in August, and rose again in September. In the treated towns there was a small increase in June and July, due partly to the emergence of DDT resistance, but by the end of August the numbers were down to the February level.

The population of this area consists in the main of two ethnic groups living separately in the towns—a "Latin-American" group, largely poor, badly housed, and with rudimentary sanitation, and an "Anglo-American" group whose members are mostly richer, with good housing and sanitation. Among the Latin-Americans in all 3 counties only 15% of the patients developing paralytic poliomyelitis were over 5 years of age, compared with 50% among the Anglo-Americans. At all ages (except the first year of life, for which the rates were equal) the attack rate was greater in the Anglo-American than in the Latin-American group.

In Hidalgo County the first cases of poliomyelitis preceded by a few weeks the seasonal increase in fly numbers, but from then onwards the increase in incidence of the disease was roughly parallel with the increase in flies, in both treated and untreated towns. However, in the rural areas and in Wallacy and Cameron Counties there was no such parallelism. Attack rates for each age group were similar in treated and untreated towns, and the number of cases occurring in the treated towns was essentially the same as the expected number calculated from the figures for untreated towns, showing that fly control did not reduce the incidence of the disease or prevent paralysis.

There were 65 paralytic cases in the Anglo-American group in Hidalgo County, of which 19 occurred in direct contacts of a preceding case; of the 68 such cases in the Latin-American group, 12 were in direct contacts. The disease developed within 5 to 27 days of contact in 29 out of the 31 cases, and within 18 days in 20 of them. The first cases in the epidemic all occurred in the same town; of the 103 cases occurring elsewhere in Hidalgo County, in 12 there was a history of direct contact with a case within this town, 9 of these 12 being the first cases to be recognized in the community concerned. In the county as a whole the attack rate was about 1 per 1,000, but among household contacts it was about 16 per 1,000. For non-paralytic cases the attack rate for all ages in the Anglo-American group (which was higher than in the Latin-American group) was 10·4 per 1,000, whereas among household contacts with a case of paralytic disease it was 197·9 per 1,000. It is inferred from these findings that, in this epidemic, personal contact was chiefly responsible for the spread of the disease. *M. Lubran*

1456. **Poliomyelitis in Hidalgo County, Texas, 1948. Poliomyelitis and Coxsackie Viruses from Flies**
J. L. MELNICK and R. P. DOW. *American Journal of Hygiene* [*Amer. J. Hyg.*] **58**, 288–309, Nov., 1953. 5 figs., 11 refs.

During the course of the 1948 poliomyelitis epidemic in Hidalgo County, Texas [see Abstract 1455], flies caught in the Latin-American quarters of 4 towns during April to November were examined for poliomyelitis and Coxsackie (C) viruses. Flies of each genus caught in one month were pooled and concentrated extracts (prepared by grinding in M/100 phosphate buffer; centrifugation, ultra-centrifugation, and resuspension in 10% monkey serum in M/100 phosphate buffer) tested for poliomyelitis virus by intracerebral injection into 2 cynomolgus monkeys and for C virus by intraperitoneal injection into young mice.

Of 120 test samples from about 100,000 flies, 18 were positive for poliomyelitis virus, and of 100 test samples for C virus, 45 were positive, positive and negative results being obtained from both large and small fly samples. Both viruses were distributed fairly evenly throughout the major genera represented—*Musca*, *Sarcophagula*, and *Phaenicia*. In addition, poliomyelitis virus was isolated from one sample mostly composed of *Callitroga macellaria*. Of 14 strains of poliomyelitis virus isolated from flies and one from pooled stools of patients with poliomyelitis, all were of Type 1 (Brunhilde). Typing by complement-fixation and neutralization tests was carried out on 32 strains of C virus, which fell into 13 antigenic types, 5 of which (Texas 1, 12, 13, 14, and 15) were new but have since been found elsewhere. C virus was isolated fairly regularly from April to October, but

poliomyelitis virus only from April to June, mostly in April and May, when there was also the greatest number of cases of the disease. *M. Lubran*

1457. **Poliomyelitis in Hidalgo County, Texas, 1948. Poliomyelitis and Coxsackie Viruses in Privy Specimens**
T. FRANCIS, G. C. BROWN, and J. D. AINSLIE. *American Journal of Hygiene* [*Amer. J. Hyg.*] **58**, 310–318, Nov., 1953. 2 figs., 10 refs.

During the 1948 poliomyelitis epidemic in Hidalgo County, Texas [see Abstracts 1455 and 1456], stool samples were taken from outdoor communal privies in the Latin-American quarters of the 4 towns from which fly samples had been obtained for isolation of poliomyelitis virus. Samples were taken at places as near as possible to a case of poliomyelitis and in control areas where neither the disease nor virus-carrying flies had been found, but the distribution of the samples was not very satisfactory. Extracts of samples from individual privies or of pooled samples were tested for poliomyelitis virus by intracerebral injection into rhesus monkeys, and for Coxsackie virus by intracerebral or intraperitoneal injection into suckling mice.

Poliomyelitis virus of Type 1 (Brunhilde) was isolated from some of the individual and pooled samples, but there was poor correlation with occurrence of the disease in the neighbourhood. Coxsackie virus was also isolated, rather more often than poliomyelitis virus. In general, there was good correlation between the isolation of poliomyelitis and Coxsackie viruses from privy samples and from flies in the same area, except in one area where 6 of 31 privy samples yielded Coxsackie virus but only 1 of 11 fly samples did so. *M. Lubran*

1458. **Laboratory Evidence of Influenza in England and Wales during the Winter of 1952–3**
PUBLIC HEALTH LABORATORY SERVICE. *British Medical Journal* [*Brit. med. J.*] **2**, 1178–1180, Nov. 28, 1953. 1 fig., 2 refs.

During the winter of 1952–3, an intensive effort was made by the Public Health Laboratory Service to detect influenza virus in as many parts of England and Wales as possible. Serological tests with influenza-A and -B soluble antigens were carried out on suitably spaced pairs of samples of serum, a rise in titre of 4 or more being considered significant. In many cases the virus was isolated.

Influenza A was first detected by isolation of the virus in mid-December, 1952. The weekly total of positive serological tests started to rise in the second week of January, 1953, reaching a peak at the end of that month. It decreased rapidly in February, continued low in March, and only one positive result was obtained in April. More than 50% of the cases occurred in the period from January 11 to February 7. The Registrar-General's weekly returns for deaths from influenzal pneumonia in 160 great towns showed a similar pattern, with the peak occurring about 14 days later. The number of claims for sickness benefit also showed a like pattern, the peak in this case occurring 7 days later. Data from these sources have been shown to give a good picture of the spread of an influenza epidemic, and were also in substantial agreement with the serological findings. The serological reactions were positive in 479 cases, and the virus was isolated in 106 cases from 62 different localities over a period of 13 weeks. The epidemic started in the south-east of England in mid-December, reached the south coast by the New Year, and the south-west and Midlands by the end of the first week in January, but cases occurring in Wales, East Anglia, and the north-west of England were not confirmed until the second week in January.

There were only 41 cases positive serologically for influenza B, and the virus was isolated in but 4 cases. This type occurred mostly in the south of England but was not widespread in any region. There was no peak in the number of cases detected; positive results were obtained mainly between mid-January and mid-May, occasional cases continued to occur up to August.
M. Lubran

1459. **Bacteriology of Air and Dust in a Maternity Hospital**
F. MARSH and H. E. RODWAY. *Lancet* [*Lancet*] **1**, 125–127, Jan. 16, 1954.

The bacteriology of the air and dust of the maternity wards of Thorpe Coombe Maternity Hospital, Walthamstow, London, where infants are nursed in a cot beside the mother's bed, was studied over a recent 3-year period.

The organisms grown on plates exposed for periods of one hour at different times of the day and night were chiefly *Sarcina*, *Micrococcus pharyngeus*, *Staphylococcus albus*, *Bacillus subtilis*, and a few others, including occasionally *Staph. pyogenes*. The average counts increased as much as 50-fold during ward activity, particularly bed-making. The evening counts were higher in winter than in spring, probably because there was less ventilation of the ward. The use of an aerosol alone did not lessen the dispersal of dust-borne organisms during ward activity. A total of 242 plates were exposed in this part of the investigation.

Dust-suppressive measures, such as damp-dusting and sweeping, the oiling of linoleum-covered and wooden floors, and the spraying of disinfectants into the air and on the blankets, were also ineffective. There was, however, a marked reduction in bacterial contamination of dust after: (1) washing the blankets in a detergent, (2) disinfecting blankets in a quaternary ammonium compound, and (3) disinfecting mattresses and pillows with a solution of formalin followed by sterilization in an autoclave. Altogether 231 plates were exposed in this part of the investigation.

A total of 1,094 swabs (600 nasal swabs from infants and 494 nasal, breast, and hand swabs from mothers) were examined. The use of detergents and of disinfecting methods, as described above, did not result in a decrease in the number of nasal carriers of *Staph. pyogenes* among the infants born in the hospital. The presence of this organism in the nostrils did not appear to be harmful. A few nasal swabs from infants were tested against penicillin, and in about two-thirds the organisms were found to be sensitive. *J. Cauchi*

Industrial Medicine

INDUSTRIAL TOXICOLOGY

1460. **Acute Inhalation Toxicity of Beryllium. IV. Beryllium Fluoride at Exposure Concentrations of One and Ten Milligrams per Cubic Meter**
H. E. STOKINGER, C. J. SPIEGL, R. E. ROOT, R. H. HALL, L. T. STEADMAN, C. A. STROUD, J. K. SCOTT, F. A. SMITH, and D. E. GARDNER. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg.*] **8**, 493–506, Dec., 1953. 22 refs.

In continuation of their previous work on the toxicity of beryllium (*Arch. industr. Hyg. occup. Med.*, 1950, **1**, 379 and **2**, 25; *Abstracts of World Medicine*, 1951, **9**, 132 and 22), the authors now describe the acute effects of the inhalation of an aerosolized aqueous solution of beryllium fluoride on dogs, cats, albino rats, albino mice, guinea-pigs, and rabbits. The experimental conditions were similar to those described in the previous papers, the concentration of beryllium fluoride was 10 mg. per c. metre in a first experiment and 1 mg. per c. metre in a second, and the periods of exposure were 15 and 207 days respectively.

The effects included pulmonary changes similar to those produced by beryllium sulphate, and a macrocytic anaemia not prevented or cured by administration of vitamin B_{12} (cyanocobalamin), "lextron" (a liver–stomach concentrate with a ferrous salt), or folic acid. There was also a decrease in the number of mature polymorphonuclear leucocytes and an increase in that of immature forms. A considerable amount of beryllium accumulated in the bones in a concentration exceeded only in the lungs and the pulmonary lymph nodes. Beryllium fluoride was found to be much more toxic than beryllium sulphate. *John Pemberton*

1461. **Serious Poisoning by Hexachloro*cyclo*hexane. Clinical and Laboratory Observations on Five Cases**
E. DANOPOULOS, K. MELISSINOS, and G. KATSAS. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg.*] **8**, 582–587, Dec., 1953. 12 refs.

There have been few reports of acute poisoning with benzene hexachloride. In the summer of 1951, 79 persons of various ages and both sexes living in the area of Carpenissi, Greece, suffered from poisoning due to the improper use of an insecticide composed of benzene hexachloride (40%) and magnesium silicate (60%), which they had sprinkled on their bedding and on the walls of their houses.

In this paper the authors describe the clinical and laboratory findings in 5 of the cases, one of which was fatal, examined in detail at the University Medical Clinic, Athens. The chief symptoms were lassitude, headache, and myalgia, followed by intestinal colic, diarrhoea, and stomatitis. Later, neurological signs appeared, including delirium, choreic and athetoid movements, tremor and convulsions, signs of upper motor neurone damage, and cerebellar signs. Optic neuritis occurred in 3 cases and one boy became blind from complete atrophy of the optic nerve. There were also electrocardiographic changes, toxic inhibition of erythrocyte maturation, an increase in blood chloride levels, a raised erythrocyte sedimentation rate, and, in the fatal case, laboratory and post-mortem evidence of liver damage. The patients were treated with "adrenal preparations", blood transfusion, vitamins B and C, and a high-protein diet. Of the 79 persons affected, 18 were seriously ill and 6 died. Convalescence in most cases was very slow. *John Pemberton*

1462. **Toxicity Studies of Acetone Cyanohydrin and Ethylene Cyanohydrin**
F. W. SUNDERMAN and J. F. KINCAID. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg.*] **8**, 371–376, Oct., 1953. 8 refs.

Ethylene cyanohydrin is a stable material, the cyanide and hydroxyl groups being attached to different carbon atoms; it is relatively non-toxic, and there is no record of industrial intoxication. Acetone cyanohydrin on the other hand, in which the cyanide and hydroxyl groups are attached to the same carbon atom, is readily dissociated into its components, acetone and hydrogen cyanide, and it is consequently a highly toxic material. The results of animal experiments, here reported from Jefferson Medical College, Philadelphia, support the hypothesis that this toxicity is due to the release of hydrogen cyanide *in vivo*. The nitrite–sodium-thiosulphate therapy in common use for hydrogen cyanide poisoning has proved effective in the treatment of rats poisoned with acetone cyanohydrin.

Two cases in which death was probably due to industrial intoxication by acetone cyanohydrin are described. *M. A. Dobbin Crawford*

1463. **Cadmium Intoxication. Clinical Report of an Acute Accidental Group Exposure**
M. L. AMDUR and R. A. CAPUTI. *Industrial Medicine and Surgery* [*Industr. Med. Surg.*] **22**, 561–566, Dec., 1953. 4 figs., 3 refs.

The authors describe 4 cases of cadmium poisoning caused by an industrial process in which metallic cadmium wire was melted and blown against a rotating spindle in order to coat the latter with the metal. Only about 40% of the metal was deposited and as there was no exhaust ventilation significant amounts of cadmium contaminated the atmosphere. The 4 workers who developed symptoms of cadmium poisoning were the process operator, a maintenance welder and his assistant, who worked about 10 feet (3 m.) away from the spindle, and a female clerical worker on the floor above, whose

desk and chair were near a ventilating duct which communicated with the workroom below in the immediate vicinity of the welding. The process began at 11.0 a.m. and was completed by 2.30 p.m., during which time about 10 lb. (4·5 kg.) of cadmium wire was used. It is believed that the operator was exposed to metallic cadmium while the other three were exposed to cadmium oxide fumes generated from the airborne cadmium as it entered the welding arc. All the patients complained of cough and pain or a sense of constriction in the chest, beginning either during or a few hours after exposure; other symptoms were malaise, nausea, vomiting, and headache. The welder, who was most severely affected, had marked breathlessness, and this was also a feature in the operator, whose symptoms, however, were less severe.

Inflammation of the fauces and nasopharynx was noted in all 4 patients and in 3 the conjunctivae were congested as well. In chest radiographs taken after exposure there was an increase in the vascular markings in all 4 cases compared with similar radiographs taken before exposure. The electrocardiogram showed sinus bradycardia in 3 cases, and in the case of the welder a P–R interval up to 0·24 second. Vital capacity, which was reduced in each case, returned to normal during the recovery period, which varied from one week to 6 weeks.

Urinary excretion of cadmium continued for periods varying from 3 to 7 weeks, depending on the severity of the symptoms.

Although the respiratory system was affected, many of the symptoms were not primarily respiratory. It is suggested that cadmium inactivates cholinesterase by combining with the sulphhydryl portion of the molecule; this would account for the bradycardia, heart block, abdominal pain, nausea, vomiting, and sense of constriction in the chest which were noted in all the cases.

After this incident exhaust ventilation was fitted to the plant and an airline helmet was provided for the operator. In spite of these precautions air samples taken in the breathing zone of the operator, but outside his helmet, revealed a concentration of cadmium in air which was about 11 times the maximum allowable [0·1 mg. per cubic metre of air]; 10 feet away from the operator the concentration was a little above the maximum allowable.

W. K. S. Moore

OCCUPATIONAL DISEASES

1464. **Interdigital Sinuses of Barbers' Hands**
A. R. Currie, T. Gibson, and A. L. Goodall. *British Journal of Surgery* [*Brit. J. Surg.*] **41**, 278–286, Nov., 1953. 19 figs., 28 refs.

The authors review an occupational condition which is more prevalent than is usually realized, since the patient seldom seeks medical advice—namely, the interdigital sinuses which occur on barbers' hands. At the Glasgow Royal Infirmary they examined the hands of 77 gentlemen's hairdressers, in 10 of whom some stage of interdigital sinus formation was present; the hands of none of 61 ladies' hairdressers showed any similar lesion. Only 18 cases have previously been recorded, and clinical details of these and of the present authors' 11 cases are tabulated.

The condition is characterized by pits and sinuses on the webs of the fingers which occur most commonly between the fore and middle fingers or middle and ring fingers of the right (cutting) hand. These are due to penetration of the skin by the short, sharp hairs which accumulate between the barbers' fingers, followed by secondary infection and granuloma formation. The mechanism whereby the hairs penetrate to the corium and even to the subcutaneous tissue is discussed. The sinuses are all lined by squamous epithelium, and the microscopical appearances of the various types of sinus are described and beautifully illustrated. Brief mention is made of other hair-bearing lesions, including scarring pseudo-folliculitis of the negro beard, postanal pilonidal sinus, and similar sinuses which have been described in the perineum, axilla, umbilicus, sole of the foot, and suprapubic area, and a plea is made for a more accurate nomenclature.

Simple prophylactic measures would prevent this condition altogether. Once developed, it is an irritating disability which may require surgical excision of a deeply situated granuloma, sometimes followed by skin-grafting.

John Huston

1465. **Radiokymography as a Method of Estimating the Effectiveness of Breathing Exercises in the Treatment of Silicosis.** (Рентгенокимография как метод определения эффективности лечения дыхательной гимнастикой больных силикозом)
V. P. Karmazin. *Гигиена и Санитария* [*Gigiena*] 14–18, No. 12, Dec., 1953. 3 figs.

Multiple-slit radiokymography was applied to the study of changes in the respiratory movements brought about by the therapeutic use of breathing exercises in 28 patients suffering from silicosis. The patterns of the serrated outlines of the diaphragm and ribs as shown in the radiokymograms were examined and compared with those from normal subjects and with previous kymograms from the patients undergoing treatment. This method permits an independent evaluation of the amount of movement of the diaphragm and the chest wall.

A. Swan

1466. **Mortality in Relation to the Physical Activity of Work. A Preliminary Note on Experience in Middle Age**
J. N. Morris and J. A. Heady. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **10**, 245–254, Oct., 1953. 2 figs., 12 refs.

In a previous report from the Social Medicine Research Unit of the Medical Research Council (Morris *et al.*, *Lancet*, 1953, **2**, 1053; *Abstracts of World Medicine*, 1954, **15**, 313) it was shown that mortality from coronary heart disease in middle age was apparently higher among men engaged in sedentary work than among heavy workers. The relation between physical activity of work and mortality from other causes has now been studied, and a preliminary report is presented of the results of an analysis of data on occupational mortality in England and Wales provided by the

Registrar-General's Decennial Supplement for 1930–2. The 70 occupational groups in the three lower social classes (III, IV, and V) were classified as " heavy ", " intermediate or doubtful ", or " light " on the basis of the physical effort involved. (The details of the classification are given in an appendix.) Average annual death rates from various causes among workers in the age groups 45–54 and 55–64 years were then calculated for each category of work in each social class.

Mortality from accidents in each age group was greatest among heavy workers and least among light workers in Classes III and IV and in all three classes combined; mortality in the group of heavy workers was slightly less than in the intermediate group. This was the only cause of death from which there was a definite excess mortality among the more arduous occupations.

The authors then picked out those causes of death from which mortality at age 45–64 in each of the three social classes was at least one-third greater among light than among heavy workers (except where such difference was confined to one occupational or industrial group. In this way coronary heart disease, cancer of the lung and pleura, diseases of the prostate, appendicitis, diabetes, duodenal ulcer, and cirrhosis of the liver were shown to be causes of excessive mortality among light workers. The authors suggest that it is unlikely that this excess mortality is primarily or only a result of change from a heavy to a light job following the onset of the disease, and although this may be a contributory factor in respect of the last three causes of death, it is shown that the excess persists in selected light occupations unlikely to attract workers suffering from these diseases. To a lesser extent, mortality from pulmonary tuberculosis and disseminated sclerosis was also found to be excessive among light workers. In the case of pulmonary tuberculosis, however, when all social classes were combined the highest mortality occurred in the intermediate or doubtful group, while the trend of mortality in persons with disseminated sclerosis in Class IV was not consistent with that in the other social classes.

The implications of these findings in terms of an association between physical effort in work and general health are considered, and it is suggested that, apart from any special factors associated with individual diseases, physical activity may be conducive to good health. *E. A. Cheeseman*

1467. Age and Work. A Study of 489 Men in Heavy Industry

I. M. RICHARDSON. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **10**, 269–284, Oct., 1953. 1 fig., 18 refs.

After reviewing various aspects of the problems involved in retaining old people in useful occupation, the author reports the results of an investigation carried out at the University of Aberdeen in which 489 working men aged 50 and over were interviewed in an attempt to answer the following questions: " (1) Are older men doing less heavy work than younger men? (2) At what age do men move to less heavy work? (3) With what factors are these moves associated? (4) What is the state of the health of older men in heavy industry? " Although it was realized that unemployed and retired workers in the same age groups should also be interviewed, the difficulties encountered proved too formidable and ultimately the survey was limited to men employed in one large and one small iron foundry and a coal-mine, these units providing a satisfactorily high proportion of " heavy " jobs. In the large foundry 244 of the 879 employees were aged 50 and over, of whom 223 were successfully interviewed; in the small foundry 68 of the 324 employees were aged 50 and over and 66 of these were interviewed; and in the mine 339 of the 1,450 employees were aged 50 and over, 200 being interviewed. In the two foundries small, non-contributory pensions were paid; in the large foundry men were encouraged to continue work until the age of 70, while in the small foundry no age limit operated. In the mine the miners' pension scheme was not then in operation, and men were encouraged to remain " so long as they retained a useful capacity for work ".

Each man's work was roughly graded as heavy, medium, or light according to his own opinion and those of supervisors and the investigator, it being admitted that " the distinction between these categories is blurred "; each man was also classified according to whether or not he had changed to less heavy work, and, if he had done so, the age at which it took place was noted. In each unit the proportion performing heavy work declined with age, while in the two larger units the proportion who had changed to lighter work was much higher in the age group 60–69 than in the age group 50–59 years, but as nothing was known about the effects of death, illness, and retirement on these proportions no firm conclusions can be drawn. It may be noted, however, that in the large foundry 48% of the workers aged 50 to 59 and 73% of those aged 60 to 69 had changed to less heavy duties, while in the coal-mine the corresponding figures were 54 and 80% respectively. In most cases the change had been made when the worker was over 50. Illness or injury was associated with over half the recorded changes to less heavy work, but in many of these cases it was probable that the men were conscious of an increasing strain imposed by continued heavy work and the general speed of industrial activity and used illness or accident as the excuse to move to lighter work. The author stresses the need for " some reduction in work tempo as age increases " and that " such reduction should not be at the expense of skill ". About one-third of all the workers at the time of interview had some disability, which in 5% severely restricted occupational activity.

[The very detailed analysis of the data provided should be studied in the original. However, the limitation of the investigation to employed men only made it impossible to give definite answers to the questions posed above, while to what extent any of the information obtained can be applied to wider industrial populations is a matter of conjecture.] *E. A. Cheeseman*

See also Pathology, Abstract 1241.

Forensic Medicine and Toxicology

1468. **Sources of Error in Taking Blood for Determination of Alcohol Content.** (Fehlerquellen bei der Blutentnahme zur Alkoholprobe)
F. J. HOLZER. *Deutsche Zeitschrift für die gesamte gerichtliche Medizin* [*Dtsch. Z. ges. gerichtl. Med.*] **42**, 409–415, 1953. 1 fig.

The author emphasizes the importance of using clean tubes when collecting blood for pathological examination for forensic purposes, quoting examples showing the deleterious effects of traces of penicillin and other substances upon biochemical examinations. He also makes some [rather naïve] suggestions about accuracy and precision in measuring the amount of blood taken.

G. F. Walker

1469. **Sudden or Unexpected Natural Death due to Ruptured Intracranial Aneurysm. Survey of 250 Forensic Cases**
T. A. R. DINNING and M. A. FALCONER. *Lancet* [*Lancet*] 2 799–801, Oct. 17, 1953. 15 refs.

The clinical history, where available, and the necropsy findings in 250 consecutive fatal cases of ruptured intracranial aneurysm were analysed at Guy's–Maudsley Neurosurgical Unit, London, the object being to determine the proportion of these deaths which could have been prevented. It is pointed out that leaking aneurysms do not, as is sometimes stated, occur chiefly in young subjects; in this series over half the patients were between 50 and 70 years of age at the time of death. The prognosis becomes less favourable with advancing years, and significantly more women are affected than men. Stress, exercise, and trauma are precipitating factors in a small proportion of cases only; usually there are no premonitory symptoms.

Multiple aneurysms were found in only 6% of the cases. Actual intracerebral haemorrhage was often present, but the number of cases in which significant atheroma and hypertensive changes were observed was surprisingly small. Subarachnoid haemorrhage was diagnosed before death in only 17 cases.

The authors discuss the possibility that with earlier diagnosis, and location of the aneurysm by cerebral arteriography, prompt surgical intervention could reduce the expected mortality of over 50% in these cases to at least 33%. *Gilbert Forbes*

1470. **Cerebral Edema and its Relation to Barbituric Acid Poisoning**
L. H. MOUSEL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **153**, 459–462, Oct. 3, 1953. 10 refs.

The author quotes evidence from the literature to support the hypothesis that cerebral oedema, by prolonging the anoxia in the brain, is probably responsible for the severe complications frequently seen in barbiturate poisoning. A therapeutic plan is presented, the basic principle of which is the osmotic withdrawal of fluid from the brain by the administration of 25% salt-poor human serum albumin.

Three cases of barbiturate poisoning in adults, all of whom recovered, are described. All the patients had first been treated with analeptic drugs and general measures, without apparent improvement. Each patient was then given the serum albumin intravenously in doses of 100 ml. and 300 ml. respectively in 2 cases and in 2 doses of 500 ml. each, separated by about 10 hours, in the third. Return of reflexes occurred at 23, 8, and 17 hours respectively after administration of the albumin, and signs of voluntary activity and consciousness followed within a few hours thereafter. There were no maniacal tendencies during their recovery and restraint was not required. One patient showed marked elevation of the body temperature (105·8° F. (41° C.)), which was present before the injection of the serum albumin and was treated with ice-packs. The author concludes with a plea for the abandonment of analeptic therapy in cases of barbiturate poisoning and for the direction of treatment towards relief of cerebral oedema and anoxia.

P. N. Magee

1471. **Alcohol–Barbiturate Synergism**
E. H. BURROWS. *South African Medical Journal* [*S. Afr. med. J.*] **27**, 1057–1059, Nov. 21, 1953. 10 refs.

In this paper from the Government Pathological Laboratories, Cape Town, the author briefly records 2 fatal cases in which death was believed to have been due to the combined action of alcohol and barbiturate drugs. In the first case, by means of chemical analysis, " the brain alcohol was estimated at 0·04% " [*sic*] and the amounts of barbiturate in the liver as 10·91 mg., in the kidneys 1·79 mg., and in the stomach 1·45 mg. In the second case the evidence was circumstantial, an empty bottle which had contained " tuinal " (a mixture of equal parts of amylo- and quinalbarbitone) being found nearby.

Evidence of the synergistic action of ethyl alcohol and barbiturate observed in experimental animals is quoted from the literature and the difficulties in correlating this with toxicity in man and with the cases here reported are discussed. The author concludes that there is an additive, possibly a potentiative, action of the two drugs, and draws attention to the danger of prescribing heavy barbiturate sedation for alcoholics, with special reference to the administration of thiopentone intravenously to obstreperous drunkards. He also advises caution in giving alcohol to psychiatric patients under sedation with barbiturates, and emphasizes once again that the possibility of barbiturate having been consumed should be borne in mind by every clinician when dealing with a case of apparent drunkenness. *P. N. Magee*

Aviation Medicine

1472. **Aero-otitis: Etiologic and Therapeutic Considerations**

B. C. TROWBRIDGE. *Eye, Ear, Nose and Throat Monthly* [*Eye, Ear, Nose Thr. Monthly*] **32**, 500–505, Sept., 1953. 4 figs., 8 refs.

The physiological and pathological effects of flight on the ear are described, with special reference to the consequences of inadequate ventilation of the middle ear during recompression. Rupture of the tympanic membrane is a rare complication of aero-otitis media. In most cases the signs and symptoms are aural pain, tinnitus, and low-tone deafness, with retraction and congestion of the tympanic membrane and a serosanguinous effusion into the middle-ear cavity. Aspiration of the middle-ear fluid following double puncture of the tympanic membrane with a fine needle is preferred to conservative treatment. It is claimed that recovery is complete in about 4 days and that the early removal of fluid prevents development of adhesions causing permanent impairment of hearing. In the author's view air travel should be discouraged when acute or chronic infection prevents normal functioning of the Eustachian tubes. In cases of recurrent aero-otitis media the possibility of mechanical obstruction should be borne in mind. *J. A. Armstrong*

1473. **Altitude Stress in Subjects with Impaired Cardiorespiratory Function. A Comparison of the Responses of Normal Subjects, Patients with Angina Pectoris, and Patients with Anemia to Hypoxia**

J. P. MARBARGER, P. H. WECHSBERG, C. V. PESTEL, G. F. VAWTER, and S. A. FRANZBLAU. *Journal of Aviation Medicine* [*J. Aviat. Med.*] **24**, 263–300 and 307, Aug., 1953. 17 figs., 38 refs.

The results are reported of an investigation of the circulatory and respiratory responses to hypoxia carried out at the University of Illinois, Chicago, on three groups of subjects: (1) 10 healthy male subjects aged 21 to 27; (2) 8 patients aged 47 to 77 with angina pectoris; and (3) 14 patients aged 26 to 70 with chronic anaemia. Each subject was studied at ground level and on exposure to simulated altitudes of 10,000 feet (3,050 m.) and 18,000 feet (5,480 m.) in a decompression chamber, comprehensive analyses of cardiac and respiratory function being carried out. The normal response to the anoxia so induced included an increase in pulse rate and stroke volume, an increase in " useful work " of the left ventricle, a fall in peripheral resistance to blood flow, a slight fall in systolic and diastolic blood pressures, and maintenance of a normal venous pressure. The respiratory rate showed a tendency to rise with the more severe stress, and the oxygen and carbon dioxide content and oxygen saturation of arterial blood fell, the haematocrit value rose slightly, and minor changes occurred in the electrocardiogram (ECG) which were rapidly reversed by oxygen administration.

In the subjects with angina the blood pressure and pulse pressure were increased on initial examination, peripheral resistance was slightly raised, and there were signs in the ECG of myocardial ischaemia. The changes on exposure to altitude resembled those observed in normal subjects with the exception of an upward trend in both arterial and venous blood pressure. Angina was experienced by some members of this group after 10 minutes at 18,000 feet, and reversal of the changes in the ECG was slower than normal on oxygen administration. In the anaemic subjects at ground level the pulse rate, stroke volume, mean arterial pressure, and venous pressure were increased, peripheral resistance was slightly raised, and arterial oxygen content reduced. Their response to altitude differed from that of the other groups only in that the venous pressure rose significantly, the left ventricular work rate rose more steeply, and the changes in the ECG were reversed more slowly. The rise in cardiac output in all groups was achieved by elevation of both pulse rate and stroke volume.

It is concluded that the risk entailed in the air transport of anaemic and anginal subjects seems slight in modern aircraft, especially if oxygen equipment is available. *D. I. Fryer*

1474. **Prophylactic and Therapeutic Values of Hydergine in High Altitude Frostbite**

L. A. HURLEY and A. R. BUCHANAN. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **95**, 423–430, Oct., 1952. 4 figs., 22 refs.

In experiments at the University of Colorado " hydergine ", a mixture of vasodilator dihydrogenated ergot alkaloids, given immediately after exposure of rats for 15 minutes to −40° C. at a simulated altitude of 25,000 ft. (7,600 m.) and continued for the next 6 days, reduced the ultimate amount of tail and foot loss by gangrene. If the drug was also given in the 24 hours before exposure a greater reduction in the extent of gangrene was obtained. *G. S. Brindley*

1475. **Neurocirculatory Collapse in Aircraft Flight. Report of a Case**

M. R. HALBOUTY and D. R. LONG. *Journal of Aviation Medicine* [*J. Aviat. Med.*] **24**, 301–307, Aug., 1953. 7 refs.

A short review of the literature on collapse attributable to exposure to low barometric pressure is followed by an account of a case which occurred during a training flight at 35,000 feet (10,700 m.) (pressurized cabin with an internal altitude of 30,000 to 32,000 feet (9,150 to 9,750 m.)). After 20 minutes at this height the instructor, an experienced pilot aged 47, noticed pain in the left arm.

This was relieved by descent to 30,000 feet, but was followed within 5 to 10 minutes by pain behind both knees and blurring of near vision. Symptoms again disappeared on descent to 25,000 feet (7,600 m.), but sweating and pallor were noticed before landing after a flight lasting 2 hours and 10 minutes. Some visual disturbance now developed and was followed by frontal headache, vomiting, disorientation, and cyanosis. No localizing neurological signs were demonstrated. Blood examination revealed moderate haemoconcentration. Treatment was by oxygen administration, infusion of plasma and 5% glucose solution, and lumbar puncture, this last being followed by symptomatic relief, after which recovery was uneventful. It is suggested that the treatment of such cases should include early lumbar puncture and withdrawal of fluid. *D. I. Fryer*

1476. **Pathological Effects of Explosive Decompression to 30 mm. Hg**

C. R. Cole, D. M. Chamberlain, B. H. Burch, J. P. Kemph, and F. A. Hitchcock. *Journal of Applied Physiology* [*J. appl. Physiol.*] **6**, 96–104, Aug., 1953. 9 figs., 5 refs.

The effects of extremely rapid decompression were studied at the Laboratory of Aviation Physiology, Ohio State University. In three experiments, each carried out on 6 dogs, the animals were decompressed suddenly from a simulated altitude of 10,000 ft. (3,050 m.) to one of 72,000 ft. (22,000 m.), about 520 to 30 mm. Hg in 0·035 seconds. Group 1 was maintained at the lowest pressure (30 mm. Hg) for 2½ minutes, then recompressed to normal ground pressure in one minute; in Groups 2 and 3 recompression was begun immediately after decompression, being completed in Group 2 in one minute and in Group 3 at " free-fall " rate, that is, in about 7 minutes, the aim being to differentiate between the effects of explosive decompression and of rapid recompression. In Groups 1 and 3, 4 of the 6 dogs in each group died during the experiments; all those in Group 2 survived. The survivors were killed immediately and macroscopical and microscopical examination of all tissues except bone carried out.

The greatest changes were found in the respiratory system, in the form of massive atelectasis, haemorrhage (most marked in the lower lobes), and patchy emphysema; these phenomena occurred in all 18 dogs. The collapse of the lungs is attributed to their failure to re-expand after the production of positive intrapleural pressure by the decompression (vapothorax) owing to haemorrhage into the air passages. Haemorrhage also took place in the region of the scar of a lung biopsy which had been performed before the experiment. Petechial and ecchymotic haemorrhages and congestion were noted in the alimentary canal and in the liver, spleen, and kidneys, cellular disruption was found in the liver, kidneys, and brain, and rupture and fragmentation of cardiac muscle fibres had occurred in all the animals. The last named is attributed to dilatation of the heart caused by venous congestion or the formation of gas bubbles, to a shock wave from the explosive decompression, or perhaps to intracellular gas formation. Bilateral severe haemorrhage into the inner- and middle-ear cavities occurred in 17 of the 18 dogs and is attributed to the explosive decompression. The tympanic membranes were intact in all cases. Bleeding into the frontal sinus in 2 animals of Group 2 is attributed to the rapid recompression. It was observed that the 2 survivors of Group 1 showed decreased auditory acuity and rotation of the head. All these changes were most marked in the dogs in Group 1, and pulmonary oedema and cyanosis were superimposed in those in Group 3. *D. I. Fryer*

1477. **Aging in Air Force Pilots**

W. R. Miles and B. M. Shriver. *Journal of Gerontology* [*J. Geront.*] **8**, 185–190, April, 1953. 6 refs.

In the study here described, in which the " critical incident technique " was employed, 851 members of aircrews in the U.S. Air Force were asked to cite cases concerning either themselves or their associates of at least several years standing in which the increase in age seemed to have produced notably poorer or better performance. Of the men interviewed (average age 29·5 years) and the colleagues reported upon (average age 31·2 years), 62% and 68% respectively were pilots. The type of question and interview procedure were determined by a similar preliminary study of 185 civilians.

Analysis of the 1,836 incidents described revealed the opinion that increased age produced better performance in 457 cases, defined as " effective " incidents, and worse performance in 1,379 cases, defined as " ineffective " incidents. These cases were divided into 5 main psychological categories with various sub-divisions; a number of the actual incidents described are quoted as examples. Of the ineffective incidents, 572 (41·5%) concerned changes in " physical abilities required for the job ", which included 379 (27·5%) reports of increased susceptibility to fatigue. There was ample evidence that increase in age and greater experience both produced decreased motivation for military flying, and also some evidence that increase in age produced increased fear of flying, though it was not clear from this study what other factors contributed to this fear.

Further analysis showed that the effect of increase in age on fighter pilots was not so adverse as on bomber pilots, and the over-all results tended to confirm that flying skill and competence continue to improve in the first few years of operational flying, but that this is followed by a period of levelling-off and subsequent deterioration, in which the advantages of experience fail to outweigh the physical and motivational changes due to ageing. *D. G. C. Gronow*

1478. **Circulatory and Respiratory Responses to Acute Hypoxia in Animals " Acclimated " to Altitude**

E. F. Beard, A. L. L. Bell, and T. W. Howell. *Journal of Aviation Medicine* [*J. Aviat. Med.*] **24**, 494–507, Dec., 1953. 4 figs., 28 refs.

1479. **The Effects of Monocular Blind Areas in Visibility from Aircraft**

G. O. Emerson. *Journal of Aviation Medicine* [*J. Aviat. Med.*] **24**, 518–522, Dec., 1953. 7 figs.

Anaesthetics

1480. **Contact Ulcer Granuloma and Other Laryngeal Complications of Endotracheal Anesthesia**
C. JACKSON. *Anesthesiology* [*Anesthesiology*] **14**, 425–436, Sept., 1953. 2 figs., 20 refs.

Certain laryngeal complications of endotracheal anaesthesia are discussed, in particular the aetiology of granuloma arising from a contact ulcer. A study of the literature reveals that tracheal intubation is rarely a cause of the condition. The vocal process of the arytenoid cartilage is the most frequent site of the lesion, because the vocal processes project into the lumen of the larynx, are in constant movement, and are covered only by a thin layer of mucoperichondrium. In the author's view the few cases of contact ulcer granuloma which do occur can be avoided by gentleness on the part of the operator and by the use of smooth, well-finished tubes.

Treatment in the early stages consists in resting the voice. If, however, a granuloma has already developed on the site of a contact ulcer, surgical removal of the tumour may be necessary. *Ronald Woolmer*

1481. **Anesthesia Techniques for Excisional Pulmonary Surgery; Experiences with Iproniazid**
H. E. SUSBAC and M. B. GENAUER. *Quarterly Bulletin of Sea View Hospital* [*Quart. Bull. Sea View Hosp.*] **14**, 110–127, July, 1953. 4 figs., 23 refs.

The anaesthetic technique employed at Sea View Hospital, New York, for pulmonary resection in advanced cases of tuberculosis is described. Intubation is performed after preliminary surface analgesia of the mouth, throat, and larynx has been produced by spraying with 4% cocaine and injection of 2 ml. of the solution into the trachea. Premedication is with $1\frac{1}{2}$ to 3 grains (0·1 to 0·2 g.) of pentobarbitone by mouth, or 2 grains (0·12 g.) of sodium phenobarbitone with $\frac{1}{200}$ gr. (0·3 mg.) of scopolamine by injection. If there is much secretion, intubation may be performed with the patient conscious; otherwise it is performed after the intravenous injection of 10 ml. of 2·5% "surital" and 40 to 100 units of "intocostrin" (D-tubocurarine), with a Macintosh laryngoscope, a cuffed tube being used and not more than 4 or 5 ml. of air introduced into the cuff. The prone position of the patient is preferred for operation, as the authors find that there is least interference with respiration and circulation in that position. Cyclopropane and oxygen are commonly used for maintenance anaesthesia, a closed-circuit circle technique with a carbon dioxide absorber being employed. To prevent the development of atelectasis respiration is assisted throughout, this usually being accomplished by the weight of the anesthetist's hand on the rebreathing bag, but is not fully controlled, even when the chest is open. Tracheobronchial suction is used as required, and before each intermittent manual inflation of the lungs. Before operation, 500 ml. of 5% glucose in water is given intravenously, followed by blood transfusion as required, and the latter is continued postoperatively to allow for loss of blood after the chest is closed; circulatory depression following withdrawal of the cyclopropane–oxygen mixture appears to be common, and administration of oxygen may be required. Pulmonary function tests are employed, and in borderline cases the ventilatory reserve (that is, the maximum breathing capacity divided by the resting minute volume) should be at least 6 (the normal figure for men being 20 and for women 13) before operation is contemplated. In 150 cases anaesthetized between July, 1951, and December, 1952, with this technique no deaths occurred during operation, nor could any postoperative death be attributed to the anaesthesia.

Since the introduction of treatment with *iso*nicotinic acid derivatives many cases formerly considered inoperable have been improved sufficiently to allow of operation being performed. The authors have noted no special hazards due to isoniazid, but describe 6 cases of hyperirritability of the nervous system following the use of iproniazid which took the form of increased reflexes, or even clonic muscular contractions, during preparation for anaesthesia; they attribute this to the effect of sympathicomimetic drugs, such as cocaine and scopolamine, and recommend that treatment with iproniazid be discontinued for at least 4 weeks before operation.

[The prone position has undoubted advantages for the anaesthetist, but sometimes presents the surgeon with technical difficulties which are not encountered in the lateral decubitus position. The technique described here is not likely to find favour with British anaesthetists.]
D. D. C. Howat

1482. **Hibernation Anaesthesia in Major Surgery. A Report of 36 Cases**
A. SMITH and J. G. FAIRER. *British Medical Journal* [*Brit. med. J.*] **2**, 1247–1248, Dec. 5, 1953. 6 refs.

The authors discuss the defensive reaction of the body to surgical trauma, pointing out that the irreversible peripheral vascular failure encountered after long surgical operations is a result of the body's attempt to preserve its *milieu intérieur*. They describe a technique for producing a state of "artificial hibernation" which they have used with success in 36 cases of major surgery at Charing Cross Hospital, London. The method is a modification of that of Laborit *et al.* (*Presse méd.*, 1952, **60**, 206), the drugs used being restricted to promethazine, pethidine, and chlorpromazine given, in the proportions advocated by Laborit, during the 30 minutes preceding operation. Anaesthesia is completed with a small dose of thiopentone, and tracheal intubation is carried out. A small dose of a relaxant is given as indicated, but respiration is unaided; oxygen is administered if respira-

tion becomes inadequate. Care is taken to replace any blood lost.

The condition of all the patients after operation was excellent; at no time was there any cause for anxiety and in none of the patients was there nausea, vomiting, or headache. Amnesia was present for 6 to 8 hours after operation, the patient being free from pain during this period.

Although hypothermia was not the object and ice-packs were not used, a fall in temperature, as expected, was noted during the procedure. *Donald V. Bateman*

1483. **Postural Ischaemia and Blood-pressure**
G. E. H. ENDERBY. *Lancet* [*Lancet*] **1**, 185–187, Jan. 23, 1954. 5 figs., 8 refs.

Postural ischaemia occurs when good venous drainage is associated with an arterial systolic pressure of about 60 mm. Hg, but the hydrostatic effect of gravity on the column of blood above or below heart level must also be taken into consideration, as this paper from the Queen Victoria Hospital, East Grinstead, Sussex, well shows.

In the conscious subject vasomotor control maintains the blood pressure constant at heart level, irrespective of posture; elsewhere, gravity induces a gradient in arterial pressure when the body is tilted or returned to the upright position, the blood pressure in the elevated parts of the body, such as the head and neck, being reduced by 30 mm. Hg for every 15 inches (38·1 cm.) of vertical height above heart level. In the dependent regions, such as the legs, pressure is raised by a similar amount. The same gradient is observed in the anaesthetized patient after autonomic paralysis with hexamethonium bromide. Thus the local blood pressure at the site of operation in the raised parts of the body is considerably lower than the blood pressure at heart level. In the reversed Trendelenburg position at 30 to 35 degrees from the horizontal the cerebral blood pressure is estimated to be 30 to 40 mm. Hg when the pressure at heart level is 60 mm. Hg. *A. M. Hutton*

1484. **Suxamethonium (Succinylcholine) Chloride and Muscle Pains**
H. C. CHURCHILL-DAVIDSON. *British Medical Journal* [*Brit. med. J.*] **1**, 74–75, Jan. 9, 1954. 6 refs.

An investigation was carried out at St. Thomas's Hospital, London, to determine whether muscle pains followed the injection of suxamethonium, the subjects being (1) a group of 32 out-patients undergoing a minor surgical operation necessitating general anaesthesia and muscular relaxation, and (2) 36 patients remaining in hospital for at least 48 hours. Premedication consisted of 10 mg. of papaveretum hydrochloride and 0·425 mg. of hyoscine hydrobromide; in patients over 60 years 0·6 mg. of atropine sulphate replaced the hyoscine. Anaesthesia was induced with 0·3 to 0·5 g. of thiopentone, followed by 30 to 150 mg. of suxamethonium.

It was found that 21 (66%) of the patients in Group 1 developed muscle pain, often severe in nature, which lasted 2 to 3 days, the pain being generalized in 13, confined to the arms and legs in 6, and subcostal only in 2. Details are given of 3 cases. Only 2 of the 36 patients in Group 2 complained of muscle pains.

To abolish muscular fasciculation 40 mg. of gallamine triethiodide was given before the suxamethonium in a further series of cases. The incidence and severity of muscle pains were reduced but not abolished, suggesting that the pains were not due to vigorous twitching of the muscles but to a combination of depolarization by suxamethonium and normal muscular activity.

The author emphasizes that suxamethonium has two serious disadvantages—namely, it has no antidote, and it is unsuitable for administration to out-patients because of resulting muscle stiffness. He suggests that the life of this drug will depend on the time taken to find a short-acting muscle relaxant acting by competitive inhibition but destroyed by plasma cholinesterase, neostigmine providing an effective antidote. *D. J. Pearce*

1485. **An Investigation of Efocaine, a Long-acting Local Anesthetic Agent. I. Animal Studies**
G. MARGOLIS, H. E. HALL, and W. K. NOWILL. *Archives of Surgery* [*Arch. Surg.* (*Chicago*)] **67**, 715–730, Nov., 1953. 6 figs., 13 refs.

A severe destructive effect of "efocaine" on rabbit tissues was demonstrated with 0·5-cc. doses, equivalent to 10-cc. doses in man. The major noxious substance in efocaine is propylene glycol, which comprises 78% of the solvent vehicle for efocaine. This material retains a destructive effect in 0·5-cc. doses, even when diluted as much as 1:8. Reduction of the dose level of efocaine to 0·05 cc. does not eliminate the necrotizing effect of this substance. This necrotizing action was confirmed by tests in dogs and rats. In the face of the functional and structural effects on nerve produced by the solvent vehicle for efocaine and by propylene glycol alone, the part the precipitated anesthetic agents in this drug play in the production of prolonged anesthesia is impossible to determine.—[Authors' summary.]

1486. **An Investigation of Efocaine, a Long-acting Local Anesthetic Agent. II. Clinical Studies**
W. K. NOWILL, H. E. HALL, and G. MARGOLIS. *Archives of Surgery* [*Arch. Surg.* (*Chicago*)] **67**, 731–737, Nov., 1953. 1 fig., 11 refs.

The prolonged anesthetic effect of "efocaine" was verified by clinical studies. Although subjective relief of pain was noted with the use of efocaine, a significant decrease in postoperative complications and in requirements for narcotics was not observed. Since anesthesia could also be produced by the efocaine solvent (78% propylene glycol and 2% polyethylene glycol 300), which contains none of the anesthetic agents, the mode of action of this drug is questioned. Complications, namely, neuritis, inflammatory reactions, and lasting absence of nerve function, resulted from the clinical use of this drug. —[Authors' summary.]

1487. **Complications following the Use of Efocaine**
D. C. MOORE. *Surgery* [*Surgery*] **35**, 109–114, Jan., 1954. 2 figs., 11 refs.

Radiology

EXPERIMENTAL

1488. **Effect of Irradiation with *X* Rays on the Permeability and Barrier Function of the Subcutaneous Connective Tissues and Lymph Nodes.** (Влияние рентгеновых лучей на проницаемость и барьерные функции подкожной соединительной ткани и лимфатических узлов)
P. N. KISELEV. *Вестник Рентгенологии и Радиологии* [*Vestn. Rentgenol. Radiol.*] 8–14, No. 6, Nov.–Dec., 1953. 3 figs., 5 refs.

Experimental irradiation of the skin and the lymph nodes of mice and rabbits with doses varying from 225 r to 1,350 r showed that in both cases irradiation produced changes in the permeability and the anti-infective barrier function of the irradiated tissues. Permeability was at first increased and the barrier function decreased, but with the progress of the reparative process both functions became normal; later still, permeability decreased while the barrier function increased. However, with doses exceeding 300 r there was no subsequent increase in the anti-infective barrier function. *A. Orley*

1489. **The Reaction of the Lung on Bronchography with Watersoluble Contrast Media in Rats. Comparison between Two Media.** [In English]
B. HELLSTRÖM. *Acta radiologica* [*Acta radiol. (Stockh.)*] **40**, 371–382, Oct., 1953. 12 figs., 7 refs.

At the Karolinska Hospital, Stockholm, the author investigated and compared the reaction of the rat's lung to the intrabronchial installation of two water-soluble contrast media containing carboxymethyl cellulose, " umbradil-viscous B " and " ioduron B ". To each of 2 groups of 40 white rats, 0·1 ml. of one of the media per 100 g. body weight was instilled into a selected lobe through a tracheotomy tube under fluoroscopic control. The animals were killed after intervals of 2 days and 1, 2, 3, and 6 months, when histological preparations were made of the treated lobe (control sections being made from the contralateral, untreated, lung) and stained selectively for carboxymethyl cellulose.

Of the 40 rats given umbradil-viscous B, 32 survived the injection. Macroscopically the lungs were, on the whole, normal, although slight congestion of both lungs was noted in a few cases and in one there was evidence of localized collapse. Microscopically, at 48 hours, the greater part of the medium had disappeared; there was slight thickening of the alveolar septa. At later stages, up to 6 months, the medium was still less evident, only occasional small residues remaining in the alveoli. The histological picture of the lung was quite normal. Of the 34 rats surviving the injection of ioduron B, 25 showed macroscopic and microscopic changes in proportion to the amount of medium injected. Major or minor degrees of collapse were found in the treated areas, and this persisted up to 6 months. A chronic inflammatory reaction of the nature of an indurated pneumonic process was observed. Histologically, the alveolar walls were thickened and infiltrated with inflammatory cells. Large quantities of opaque medium persisted in the lungs.

The author suggests that the greater viscosity of ioduron B may be a factor in the production of these results. He emphasizes that the findings are not necessarily applicable to man, in whom further studies would seem to be desirable. *A. M. Rackow*

1490. **The Concentration of Oxygen Dissolved in Tissues at the Time of Irradiation as a Factor in Radiotherapy**
L. H. GRAY, A. D. CONGER, M. EBERT, S. HORNSEY, and O. C. A. SCOTT. *British Journal of Radiology* [*Brit. J. Radiol.*] **26**, 638–648, Dec., 1953. 9 figs., 23 refs.

It is known that the damage caused to both normal and malignant tissue by a dose of x or γ radiation is less if it is poorly oxygenated than when it is well supplied with oxygen, though this does not hold good for neutrons. The effectiveness of x-ray treatment might therefore be increased if the subject were to breathe oxygen at the time of irradiation. Experiments carried out at Hammersmith Hospital, London, on mice bearing the Ehrlich ascites tumour are described in which it was shown that the tumour regression produced by a given dose of x rays was greater, and the dose required to produce a given degree of regression reduced by one-third, when the animals were breathing pure oxygen in place of air. Some evidence was obtained that even more favourable results could be obtained if the oxygen were supplied at higher pressures, but only at the risk of lung damage. The effect of oxygen treatment on the response of the tumour was much greater than on that of skin and hair, as would be expected since the latter are normally well supplied with oxygen. Experiments on chick fibroblasts exposed to x rays *in vitro* showed a similar relationship between radiosensitivity and oxygen tension, and in one of two chemical models investigated a closely comparable dependence of the amount of change caused by a given dose of x rays and the concentration of dissolved oxygen was found.

The authors suggest that oxygen exerts an influence on the biological response to x rays by affecting the chemical changes produced directly in the cell by irradiation. The degree of injury produced in tumour cells by chemical agents such as nitrogen mustard is completely independent of oxygen concentration, which supports the theory that the mode of action of such agents is different from that of x rays.

While these findings suggest that oxygen treatment may be of value in clinical radiotherapy, they give no indication that in man any particular type of neoplasm would respond more favourably to x rays if the patient were breathing oxygen. The authors conclude, however,

that " the possibility of substantial differential gain in effectiveness of the radiation with respect to tumour tissue relative to well-oxygenated normal tissue is inherent in any situation in which regions of partial anoxia occur in a human tumour ". *J. Walter*

RADIOTHERAPY

1491. **Radiation Therapy of Malignant Lesions about the Eye**

M. D. SCHULZ and C. G. STETSON. *Radiology* [*Radiology*] **61**, 786–795, Nov., 1953.

Carcinoma of the eyelid is the most common tumour occurring in the region of the eye, forming about 60% of all primary tumours in this region seen at the Tumor Clinic of the Massachusetts General Hospital and Eye and Ear Infirmary, Boston. Among the remainder, few of which are ever seen by the radiotherapist, angiomata account for some 15% of all orbital tumours; they behave in the same way as angiomata in general, and involution of the capillary type may be accelerated by moderate-dose radiotherapy. Lymphoma sometimes occurs in the orbit as an episcleral or conjunctival infiltration and may be unconnected with lymphomatous disease elsewhere, so that long periods of freedom may follow surgery or *x*-ray treatment with doses of 200 or 300 r daily up to 600 to 900 r. Unilateral exophthalmos may be due to lymphoma deep in the orbit, in which case surgical exploration is necessary for diagnosis. Seven out of 16 patients with orbital lymphoma treated with *x* rays survived for 5 years, though not all without local recurrence or manifestation of the disease elsewhere. Tumours of the lacrimal gland are slow-growing, silent tumours which invade bone. They are analogous to mixed salivary tumours and if not completely removed recur with increasingly malignant tendencies. The more undifferentiated type of tumour is sensitive to *x* rays in doses of the order of 2,000 r, but there is no record of a permanent cure with radiotherapy. Sarcomata of the orbital tissues are uniformly radioresistant.

Carcinoma of the eyelid is essentially a carcinoma of the skin, but presents special problems because of its location. It is more common in men than women, and usually occurs after 40 years of age. Of 400 such tumours seen over a 17-year period, 85% were basal-celled, 12% squamous-celled, and 3% were mixed carcinomata. The lower lid was involved in 45% of these cases, the inner canthus in 20%, the upper lid in 15%, the outer canthus in 10%, and combinations of these in 10%. Treatment, to be successful, must not only control the disease, but also give a satisfactory cosmetic result, and protection of the eye by means of lead shields is of course essential. For purposes of *x*-ray treatment four categories are defined. (I) Small, non-infiltrative lesions which respond to 2,400 to 2,700 r given in one dose, or to 4,500 r fractionated over a week. (II) Infiltrative lesions confined to the lid should receive fractionated radiotherapy, 4,500 r in one week, except where a plastic repair is likely to be necessary, when it may be better to excise the tumour and forgo *x*-ray treatment. (III) Tumours invading the orbit, globe, or bone should receive *x*-ray treatment first, followed by surgery if the disease is not controlled. (IV) For extensive disease, with or without metastases, palliative radiotherapy may be effective.

It is imperative that control of the disease should be secured at the first attempt, and this should be possible in 80% of cases in Classes I and II. The most common cause of failure, which is manifest during the first year as a rule, is inadequate treatment, but the likelihood is greater in cases of squamous-celled than of basal-celled carcinoma. Cataract is the most important complication of treatment. The human adult lens can tolerate 800 r, and proper shielding should prevent such a dose reaching the lens. A long latent period may intervene between treatment and the appearance of the cataract.

I. G. Williams

1492. **Radiation Therapy in Carcinoma of the Thoracic Esophagus**

D. C. ADLER and P. H. DEEB. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **70**, 709–720, Nov., 1953. 10 figs., 13 refs.

The authors draw attention to the tendency among radiologists in the U.S.A. to regard *x*-ray therapy as of little value in the treatment of carcinoma of the oesophagus. This tendency is due partly to the poor results which have been obtained with radiotherapy and partly to recent advances in thoracic surgery. In view of this, they report 3 cases of carcinoma of the oesophagus treated at the White Memorial Hospital, Los Angeles, with a combination of *x*-ray therapy and intracavitary radium.

The patients, a woman and 2 men, were aged 73, 68, and 59 respectively and all had squamous carcinoma of the oesophagus the duration being 6, 6, and 2 months respectively. In all cases *x*-ray therapy, given for several months, was followed by intraoesophageal radium therapy, given at a distance of 1 cm. The patients lived for 17, 34, and 25 months respectively after treatment, and at necropsy in the first 2 cases no trace of residual tumour in the oesophagus could be found. The third patient died suddenly of heart disease and no complete necropsy was performed.

The authors review the literature of similar cases and conclude that there is a definite place for radiotherapy in the treatment of carcinoma of the oesophagus.

R. D. S. Rhys-Lewis

1493. **Clinical and Technical Aspects of the Radiotherapy of Carcinoma of the Oesophagus.** (Ein klinischer und methodischer Beitrag zur Strahlentherapie der Oesophagus-Karzinome)

H. J. FIEBELKORN and E. SCHERER. *Strahlentherapie* [*Strahlentherapie*] **92**, 383–394, 1953. 10 figs., 31 refs.

The authors review the results in 110 cases of inoperable carcinoma of the oesophagus treated by radiotherapy at the Strahleninstitut, University of Marburg, between 1942 and 1952. Three main methods of treatment were employed: (1) 53 cases were treated by a

"cross-fire" technique using multiple small fields of a size up to 6×8 cm., and given 300 r per field daily to a total tumour dose of 2,000 r; (2) 18 cases were treated by the cross-fire method supplemented by intracavitary radium introduced into the oesophagus under fluoroscopic control; and (3) the remaining 39 cases were treated by continuous rotation therapy to a total tumour dose of 5,000 r in 20 to 30 days.

The best results, with at the same time the least constitutional disturbance and negligible skin reaction, were obtained by the rotation technique. The average survival periods for the three groups were 5, 7, and 8 months respectively. *Jan G. de Winter*

1494. **Intracavitary Use of Colloidal Radioactive Gold**
G. A. ANDREWS, S. W. ROOT, R. M. KNISELEY, and H. D. KERMAN. *Radiology* [*Radiology*] **61**, 922–929, Dec., 1953. 6 figs., 10 refs.

Colloidal radioactive gold (^{198}Au), which is a beta and gamma emitter, has been used at the Institute of Nuclear Studies, Oak Ridge, Tennessee, for the past 2 years in the intracavitary treatment of pleural and peritoneal effusions due to neoplasms. Doses of 75 mc. are instilled into the pleural cavity and of 150 mc. into the peritoneal cavity, the solution being run into the cavity through a polythene tube passed through the needle after aspiration of a considerable proportion of the effusion. In a few cases this was repeated after an interval of several weeks. Where it is necessary to treat more than one cavity, this is carried out separately at intervals of a few weeks, and dosage is adjusted to keep the total within the limits of tolerance. The concentration of ^{198}Au in the effusion decreases rapidly in the first 4 days after injection owing to adsorption on the serous surface. Regional lymph nodes show little activity; up to 1% of the given dose may be detected in the blood for the first 10 days, but the amount recovered from the urine has never exceeded 1%. The liver, spleen, and bone marrow have been shown at necropsy to contain up to 15% of a dose of ^{198}Au given intraperitoneally, and in the dog 90% of the ^{198}Au in the blood has been found to be removed on its first passage through the liver. However, transfer to these organs occurs only gradually. Several weeks elapse after giving the isotope before there is a reduction in the accumulation of fluid. From the second to the fourth or fifth day after the injection mild radiation sickness frequently occurs; in addition a few patients develop leucocytosis, some leucopenia, and all lymphopenia.

The effect of ^{198}Au is usually considered to be due to the beta radiation, but the possibility is mentioned that gamma emission may be more important in the irradiation of lymph nodes, liver, spleen, and bone marrow than has been realized. The mechanism of its action is unknown; persistence of malignant cells is variable and fibrosis insignificant. This method of treatment is suitable for patients with symptoms caused by the effusion, but with no large masses and in fairly good general health. Mention is also made of the postoperative prophylactic use of ^{198}Au.

The short-term results of treatment in 39 cases indicate a distinct decrease or cessation of accumulation of fluid in 16, some decrease in 7, and no effect in 2, 10 cases being unsuitable for assessment because of early death from neoplasm and another 4 because combined treatment had been given. On this basis the authors consider intracavitary colloidal ^{198}Au to be more valuable than *x* rays in the treatment of malignant effusions.

G. E. Flatman

1495. **The Late Results of Combined Surgical and Radiological Treatment of Mammary Carcinoma.** [In English]
P. J. L. SCHOLTE, G. KORTHOF, and W. F. SUERMONDT. *Archivum chirurgicum neerlandicum* [*Arch. chir. neerl.*] **5**, 317–328, 1953. 15 refs.

1496. **The Non-surgical Treatment of Basal Celled Carcinoma (Rodent Ulcer)**
D. S. ANDERSON. *Transactions of the St. John's Hospital Dermatological Society* [*Trans. St John's Hosp. derm. Soc. (Lond.)*] No. 32, 25–32, Oct., 1953. 3 figs., 2 refs.

An account is given of 83 cases of rodent ulcer treated between 1946 and 1948 at St. John's Hospital for Diseases of the Skin, London, by means of either unfiltered radium or low-voltage *x* rays. Radium plaques of two strengths were available, a full-strength applicator measuring 1·4×1·4 cm. and containing 5 mg. of radium per sq. cm., which gave a surface dosage of 61 r per minute, and a half-strength applicator 2 cm. square containing 2·5 mg. of radium per sq. cm. and giving 29 r per minute. Usually the full-strength plaque was applied for 3 hours, giving a surface dose of 11,180 r; in several cases this dose was repeated 2 to 4 weeks later. *X*-ray therapy was given at 90 kV through circular applicators 1 to 5 cm. in diameter at 22 cm. F.S.D. In most cases a single dose of 1,500 r was given initially, and a further dose of 1,200 to 1,500 r given 3 weeks later.

Of the 83 cases treated, the disease recurred within 5 years in 19%. This high recurrence rate is admitted to have been due to the methods of treatment used, and the techniques have now been revised. Radium treatment has been abandoned, and *x*-ray therapy is given either as a single-dose treatment of 2,500 r or as a fractionated course to a total dose of 6,000 r in 10 daily treatments of 600 r each.

[It is gratifying to learn that the generally accepted policy of referring all malignant dermatological cases to a cooperating Radiotherapy Centre for treatment has now also been adopted by this hospital.]

Jan G. de Winter

1497. **Lymphogranulomatosis of the Small Intestine.** (О лимфогранулематозе тонкого кишечника)
S. B. ZAKOV. *Вестник Рентгенологии и Радиологии* [*Vestn. Rentgenol. Radiol.*] 42–49, No. 5, Sept.–Oct., 1953. 6 figs., 25 refs.

In the author's experience lymphogranulomatosis of the small intestine is not uncommon, 13 cases having been diagnosed radiologically, and subsequently confirmed, within a period of 3 years. In all cases the radiological appearances were typical and the course of the

disease was malignant. The sites most commonly affected were the duodenum and the proximal part of the jejunum. In view of the high sensitivity of lymphogranulomatous infiltration to radiotherapy, the effect of a trial irradiation may help to confirm the diagnosis in cases difficult to diagnose otherwise.

Treatment should be based primarily on radiotherapy, but other, complementary, therapeutic methods should not be neglected. Early recognition of the lesion and adequate therapy may considerably prolong the life of the patient. *A. Orley*

1498. **Osseous Damage in Irradiation of Renal Tumors in Infancy and Childhood**

W. M. WHITEHOUSE and I. LAMPE. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **70**, 721–729, Nov., 1953. 4 figs., 11 refs.

It has long been recognized that the rapidly developing bones of the young are peculiarly susceptible to damage by radiation, even in small doses. Most studies have been made on the long bones and there have been few reports of damage to the vertebral column. In this paper the authors report 4 cases of vertebral damage in young patients treated by radiotherapy at the University of Michigan Hospital, Ann Arbor, for Wilms's or other renal tumours. In all cases irradiation was confined to one side of the abdomen.

The first patient, a girl aged 3 years, was given 1,850 r to each of two fields 15×10 cm. over 13 days, and the second, a female infant aged 10 months with a renal teratoma, received 2,600 r to each of two fields 20×8 cm. over 35 days and subsequently underwent nephrectomy. When seen 14 and 10½ years later respectively, both patients had marked scoliosis and underdevelopment of the right ilium. The other 2 patients, both boys, one aged 13 months and the other 4 years, received respective doses of 1,900 r over 19 days and 2,300 r to each of two opposing fields 12×10 cm. in 32 days. When reexamined after 11 years these 2 patients were found to have only minimal changes in the vertebral bodies and ilia.

The authors conclude that it is difficult to assess accurately the dosage received by the vertebral bodies, but it seems that the damage is less likely to occur when irradiation is given to small than to large fields. Furthermore, the younger the patient and the more intense the radiation, the more likely is damage to occur. It also seems, from the survival of the 4th patient, that very intense radiation need not be given to control the disease, although no histological verification of residual neoplasm was obtained in that case. *R. D. S. Rhys-Lewis*

1499. **Renal Sclerosis, " Post-radiation Nephritis " Following upon Irradiation of the Upper Abdomen**

H. RUSSELL. *Edinburgh Medical Journal* [*Edinb. med. J.*] 60, 474–483, Dec., 1953. 13 figs., 18 refs.

In this paper from the Christie Hospital, Manchester, 4 cases of the fully established syndrome of " post-radiation nephritis " are described in detail. All the patients were males between the ages of 25 and 46. Irradiation of the upper abdomen had been carried out for seminoma in 3 cases and for retroperitoneal carcinoma in one, the dosage varying between 2,700 and 3,000 r given over periods of 3½ to 5 weeks. The survival time after treatment ranged from 13 to 25 months. The classic clinical features of albuminuria, severe anaemia, progressive renal failure, and hypertension were present in all cases. Post-mortem examination of the kidneys showed a diffuse interstitial fibrosis and extensive tubular degeneration, whereas glomerular damage, although constantly found, was less marked; other, less constant, findings included perirenal sclerosis and arteriolar necrosis.

A review of the pathological records of the hospital over the previous 10 years revealed two cases in which death had occurred at an earlier stage of the disease. The first of these patients, a male aged 33, died of pulmonary infarction 8 days after starting *x*-ray treatment, the kidneys having received about 1,500 r. On microscopical examination they showed a generalized interstitial oedema and well-marked capillary dilatation. The second patient, a woman of 45, received a dose of at least 2,000 r to the renal area in 30 days. Post-mortem findings 8 months later included subcapsular sclerosis and arteriosclerotic changes in the kidneys, but the picture was complicated by para-aortic metastases and a unilateral hydronephrosis.

The author discusses the various factors which may be of importance in the production of *x*-ray nephritis. From a consideration of the microscopical findings she concludes that renal irradiation produces a diffuse serous inflammation with prolonged capillary dilatation and circulatory stasis. Irreversible mesenchymal damage follows, with progressive fibrosis of the kidney.

A. M. Jelliffe

RADIODIAGNOSIS

1500. **The Arnold–Chiari Malformation. Radiological Examination with the " Ziedses des Plantes " Procedure**

H. VERBIEST. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **16**, 227–233, Nov., 1953. 8 figs., 14 refs.

The literature on the radiological diagnosis of the Arnold–Chiari malformation is reviewed and brief reference is made to the limitations for this purpose of ordinary radiological examination of the skull and spinal column, myelography, and lumbar pneumoencephalography. The author then describes the results obtained with ventriculography in 11 cases of the Arnold–Chiari malformation at the Neurological Clinic of the State University of Utrecht. In all the cases air was introduced into a lateral ventricle and manipulated into the fourth ventricle according to the method of Ziedses des Plantes (*Acta radiol.* (*Stockh.*), 1950, **34**, 399). The patients in this series included 6 infants under one year of age and 5 adults.

The presence of the malformation was demonstrated by air ventriculography in 8 of the 11 cases; in one of the remaining 3 there was a dilated and obstructed

ventricle, in another insufficient filling, and in the third a concomitant stenosis of the aqueduct. It is pointed out that in this last case stenosis of the aqueduct could not have been recognized if myelography or lumbar pneumoencephalography only had been carried out, and that operative decompression of the Arnold–Chiari deformity would not only be unsuccessful but might increase symptoms. Of the radiological findings characteristic of the Arnold–Chiari syndrome, elongation of the fourth ventricle was best seen in a lateral film taken with a horizontal ray and the patient in the prone position, while cerebellar herniation into the spinal canal was also best seen in the lateral projection, but only in cases with a good communication between the fourth ventricle and the spinal subarachnoid space.

Hydrocephalus was present in all the infants, and 4 of the adults had dilated ventricles, but only in one case was the intracranial pressure increased. The possible causes of the hydrocephalic changes are discussed, particular reference being made to 4 cases in which the fourth ventricle communicated freely with the basal cisterns, but not with the spinal subarachnoid space, and 3 in which there was free communication between the fourth ventricle and both the basal cisterns and the spinal subarachnoid space. *W. B. D. Maile*

1501. **Indications for and Results of Vertebral Angiography in Neurosurgery.** (Indications et résultats de l'angiographie vertébrale en neuro-chirurgie)
D. Petit-Dutaillis, B. Pertuiset, J. Rougerie, and P. Namin. *Presse médicale* [*Presse méd.*] **61**, 1499–1503, Nov. 18, 1953. 11 figs., 16 refs.

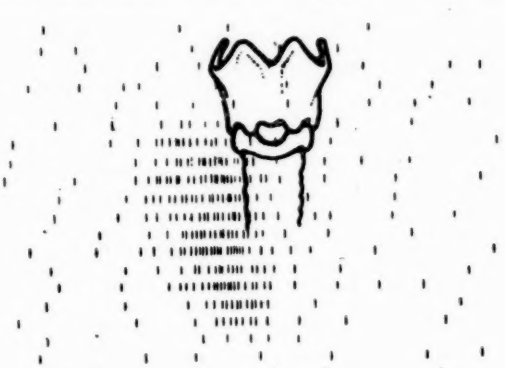
Further to their paper describing their method of angiography by the anterior cervical route (*Presse méd.*, 1952, **60**, 1415; *Abstracts of World Medicine*, 1953, **13**, 350) the authors now discuss some of the incidents and accidents which they have encountered, and the indications for the method. In a total of 162 cases examined, 4 serious accidents occurred, 2 of which were fatal. In the first case the injection of 5 ml. of 1% procaine intra-arterially because of vascular spasm was followed by coma and death within a few hours; the accident was attributed to the drug and not to the method. In the second, after right vertebral angiography for a left hemianopia the patient developed a left hemiplegia which eventually recovered spontaneously. The accident was thought to have resulted from giving the injection with too great a pressure in a patient with unusually fragile vessels. In the third case hemiparesis was observed on the day following a vertebral angiography carried out to determine the cause of a meningeal haemorrhage which had occurred a month after performing carotid angiography; no cause was found, and the patient recovered. The fourth patient was elderly and had arteriosclerosis. Three days after the injection she collapsed and died with acute precordial pain. A diagnosis of myocardial infarction was made, but there was no evidence of this at necropsy. The part which angiography played in this accident was doubtful. The authors consider that absolute contraindications to angiography are hypertension, vascular sclerosis, coronary disease, renal insufficiency, and asthma, the last named on account of the risk of allergy.

The indications for vertebral angiography are (1) vascular lesion and aneurysm, and (2) intracranial tumours. Spontaneous meningeal haemorrhage with a normal bilateral carotid angiogram is regarded as the main indication. The results in cases of cerebellar tumour are often unhelpful, but for tumours at the cerebellopontine angle the results are sufficiently good to justify angiography whenever the diagnosis is in doubt. A further important indication for angiography is in the identification of deep midline tumours.

John H. L. Conway-Hughes

1502. **The Diagnosis of Morphologic Abnormalities of the Human Thyroid Gland by Means of I^{131}**
F. K. Bauer, W. E. Goodwin, R. L. Libby, and B. Cassen. *Radiology* [*Radiology*] **61**, 935–937, Dec., 1953. 6 figs., 9 refs.

A method of studying some of the morphological characteristics of the thyroid gland of patients suffering from thyroid disease, which has been developed at the Wadsworth General Hospital and University of California, Los Angeles, is described. After administration of a dose of radioactive iodine (^{131}I) the radioactivity in different parts of the gland is measured with a directional scintillation counter, which has much greater collimation than the wide-angle counter normally used for tracer studies, and records the activity from a very limited area. It is therefore necessary to give a large dose of ^{131}I, and the examination is carried out 24 to 48 hours after the ingestion of 100 to 300 μc., it being necessary to have 60 to 80 μc. concentrated in the gland. By scanning the neck systematically with the instrument, the tissue in which the isotope has accumulated can be mapped out accurately in the form of a " scintigram " [see figure].



Scintigram of a "toxic" thyroid adenoma. Note the lack of accumulation of ^{131}I in the remainder of the gland.

This method of investigation is of value in hyperthyroidism—particularly for the location of toxic nodules and for observing shrinkage after treatment with ^{131}I. In patients with recurrent hyperthyroidism after thyroidectomy the situation and amount of remaining thyroid tissue can be determined, while aberrant thyroid tissue

or a retrosternal extension of a simple goitre can be traced and the presence of solitary or multiple nodules demonstrated. In carcinoma of the thyroid the procedure is helpful in outlining both primary and secondary lesions. Where there is sufficient uptake of iodine the procedure has proved extremely valuable in the estimation of the weight of the gland by means of the formula of Allen and Goodwin.

A number of illustrative scintigrams are reproduced.

G. E. Flatman

1503. **A Noteworthy Sign for the Radiological Diagnosis of Chronic Lung Abscess.** (Ein beachtenswertes Zeichen für die Röntgendiagnose des chronischen Lungenabszesses)

G. LIESS. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortsch. Röntgenstr.*] **79**, 613–622, Nov., 1953. 12 figs., 6 refs.

The author, writing from the Charité Radiological Institute, Berlin, suggests that an important radiological sign of chronic pulmonary abscess is the demonstration of an air-filled space between the abscess wall and its contents. He explains how this gap is produced, describes 5 cases, all confirmed by operation, in which the sign was observed, and points out the value to the surgeon of precise preoperative knowledge of the type and site of such an abscess. In view of the small number of cases the suggestion is put forward somewhat tentatively.

A. Orley

1504. **Mediastinal Phlebography. A Bilateral Simultaneous Injection Technique.** [In English]

V. GVOZDANOVIĆ and B. OBERHOFER. *Acta radiologica* [*Acta radiol.* (*Stockh.*)] **40**, 395–407, Oct., 1953. 8 figs., 13 refs.

Working at the University of Zagreb, Yugoslavia, the authors have devised a technique by which very satisfactory visualization of the large veins of the superior mediastinum has been obtained by simultaneously injecting both antecubital veins with 20 ml. of a 35% solution of diodone. The method has considerable advantages over unilateral injection, notably, great pressure in making the injection is unnecessary owing to the double port of entry, a relatively low and well tolerated concentration of the opaque medium can be employed, and the medium is not diluted by influx from the contralateral vein. It is also claimed that the danger of thrombosis is decreased.

When this method is employed, a single film taken at the end of the injection often suffices for diagnosis, although more information may be obtained by taking three further serial films at intervals of one second. In the reproductions of phlebograms which accompany the paper both innominate veins and the superior vena cava are well shown. Other conditions illustrated include deviation of one or both innominate veins by enlargement of the thyroid gland, obliteration of one or more large veins by inflammatory thrombosis, distortion and thrombosis of veins caused by the presence of a tumour in the lung or mediastinum, and the demonstration of various collateral circulations.

A. M. Rackow

1505. **Coarctation of the Aorta. The Roentgenologic Aspects of One Hundred and Twenty-Five Surgically Confirmed Cases**

R. D. SLOAN and R. N. COOLEY. *Radiology* [*Radiology*] **61**, 701–721, Nov., 1953. 13 figs., 35 refs.

The authors state that out of 125 cases of coarctation of the aorta at the Johns Hopkins Hospital, Baltimore, 111 were of the type permitting resection and end-to-end anastomosis; in 10 cases this was not feasible, the length of the coarctation or the atheromatous changes making more extensive resection necessary; in 2 the lesion involved, or was proximal to, the left subclavian artery, while in 2 others there was extensive narrowing in the distal aorta.

Rib-notching, which is the most important radiological sign and is present in the majority of patients over 20, was observed in 88 cases. In 3 cases it was noted on the superior border of the rib, while in the 2 cases in which the origin of the left subclavian artery was involved it was confined to the right side. The youngest patient with this sign was 5 years old. The double aortic knuckle (figure-3 sign) was found in 33 cases. In 73 cases there was no obvious aortic knob, a striking feature in adults with a prominent ascending aorta (40 patients in this series), but less so in the young. Vigorous pulsation was often seen in the ascending aorta, and barium swallow sometimes revealed oesophageal displacement by a dilated post-stenotic segment. In 67 cases there was definite left ventricular prominence.

Angiocardiography was performed in 47 cases and aortography in 18; in 5 cases both procedures were carried out. It is considered that aortography is superior to angiocardiography for demonstrating the site of the coarctation, but that it carries more risk, 2 cases (not in the present series) being cited in which death occurred, due respectively to injection of contrast medium into the left common carotid artery and haemorrhage from the operation incision. In the authors' view operation is possible in 90% of cases of coarctation of the aorta (in 95% if aortic grafts are available), and angiocardiography or aortography should be carried out only in those cases in which the site of the coarctation is thought to be atypical. Radiological examination in the postoperative period may reveal a haematoma at the anastomosis or pleural opacity due to haemorrhage.

[Unilateral left-sided rib notching may occur, though very rarely, if there is an associated anomalous origin of the right subclavian artery distal to the stenosis or atresia.]

Kenneth A. Rowley

1506. **Radiological Studies of the Mucosal Pattern of the Stomach. Part I.** (Röntgenuntersuchungen des Magenfeinreliefs. I. Mitteilung)

W. FRIK and A. ZEIDNER. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **79**, 681–692, Dec., 1953. 15 figs., 39 refs.

There has long been disagreement as to whether the gastroscopic and radiographic appearance of prominence of the areae gastricae (*état mamelonné*, mamelonation) is indicative of a form of gastritis (the " gastritis granularis " of Bücker). This report of an investigation

carried out in Henning's clinic at Würzburg supports conventional German gastroscopical teaching that the areae gastricae are normal, and that it is only when they are unduly coarse or rigid that they tend to be associated with hypo- or achlorhydria and with symptoms, although it is pointed out that rigid statistical proof of this thesis cannot be obtained by radiological means because an excess of acid secretion in the stomach makes adequate examination impossible. Another difficulty is that gastroscopy and biopsy are largely limited to the upper two-thirds of the stomach, whereas the best radiographs are obtained of the antrum.

In a series of 1,004 [? consecutive] barium-meal examinations the granular pattern was shown 349 times, in 30 cases the mucosa was believed to be non-granular, and in the remaining 625 cases the examination was technically unsatisfactory, either because the patient was too heavily built or because there was an excess of resting juice and mucus. Towards the end of this series, however, the proportion of cases in which the pattern could not be shown was reduced, with practice, to about one in three. The importance for the visualization of the mucosal pattern of using a watery suspension of barium without added colloids and of giving an exposure of not more than 0·04 to 0·06 second is stressed. The areae gastricae are usually said to measure 0·5 to 3·0 mm. in diameter, or according to some anatomists 1 to 6 mm. The cases in this series could be subdivided into six groups, the first consisting of 39 cases with a fine mucosal pattern of oval areas measuring 0·5 to 1·5 mm. and the second of 188 cases with round or polygonal areas 1·5 to 2·5 mm. in diameter, while the remaining four groups had coarser or more rigid mucosal patterns which in 5 cases were definitely polypoid. Patients in these last four groups tended to be older and to have a lower acidity and more persistent symptoms. The authors are duly cautious about drawing conclusions until they have examined larger numbers of healthy persons with no digestive symptoms. *Denys Jennings*

1507. **Gastric Ulcer—Benign or Malignant. Preliminary Report of a Roentgenologic Study**
F. Abbot and S. Blank. *New England Journal of Medicine* [*New Engl. J. Med.*] **249**, 722–726, Oct. 29, 1953. 7 figs., 10 refs.

During a 3-year period, 22 out of a consecutive series of 50 gastric ulcers of all types diagnosed radiologically at Waterbury Hospital, Connecticut, were examined histologically. The 3 dogmatic *x*-ray diagnoses of carcinoma were all confirmed, as were 2 out of 3 diagnoses of " probable carcinoma ". Of the remaining 16 cases, in which the ulcer was demonstrated histologically to be benign, 8 had been diagnosed radiologically as benign, 4 as probably benign, and in 4 cases the radiologist refused to commit himself. Radiological diagnosis was based on the following points. (1) Whether the floor of the ulcer projected beyond the limits of the stomach after making allowances for the filling defect caused by the oedematous margin. (2) Smoothness of the margin was taken as evidence of oedema, and irregularity was considered suspicious. (3) Radiating folds extending " right up to the ulcer " were considered to be a benign characteristic. (4) Overhanging edges were considered to indicate a benign ulcer. (5) Slight irregularity of the floor was disregarded, but if it was " more than minimal " the ulcer was considered to be cancerous. (6) A triangular shape was regarded as characteristic of a healing benign ulcer.

[The limitations of these points as a basis for diagnosis are not mentioned. Diagnosis is easy with adequate films, but is inevitably less sure if it is impossible to get the ulcer in true profile or to exert controlled compression, or if the ulcer is in the horizontal part of the stomach or high up under the costal margin. Moreover, it is not so very rare for a benign ulcer to form just above an early, invisible, neoplasm.] *Denys Jennings*

1508. **Cholecystography in Infants**
R. C. Harris and J. Caffey. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **153**, 1333–1337, Dec. 12, 1953. 5 figs., 8 refs.

It is first pointed out that *x*-ray examination of the gall-bladder of infants has been consistently unsatisfactory and of little value in the diagnosis of lesions of the biliary tract. Satisfactory cholecystograms are usually obtained only in patients over 3 years of age. The results of *x*-ray examination of the gall-bladder in 25 infants under 3 years at the Babies Hospital, New York, are then described.

Three of the patients received sodium acetrizoate intravenously and the remainder either iodoalphionic acid or iopanoic acid (" telepaque ") by mouth in a dose of 0·15 g. per kg. body weight. Radiographs taken hourly showed that the gall-bladder shadow was most distinct between 4 and 9 hours after administration of the contrast medium. The best results were obtained with iopanoic acid, except in one baby of 38 days and one of 3 months; in the latter case three further doses were given at intervals of 12 hours, the gall-bladder shadow being visible between 6 and 9 hours after the last dose.

[The clinical application of the examination in infants is not discussed. In the abstracter's experience it is rarely asked for or likely to be of value. The abstracter has obtained a good concentration with approximately 0·75 g. of iopanoic acid without any unpleasant effects in a boy aged 2 years.] *Sydney J. Hinds*

1509. **Roentgenologic Observations in Hemorrhagic Fever**
D. W. S. Stiff and G. M. Powell. *Radiology* [*Radiology*] **61**, 807–813, Nov., 1953. 6 figs., 6 refs.

A number of cases of haemorrhagic fever occurring in Manchuria and Eastern Siberia were reported in the Japanese and Russian literature between 1932 and 1944, but after that date none was recorded until the disease broke out, with a total of 1,016 cases, among the United Nations Forces in Korea. The Japanese and Russian workers claimed to have established that the disease was due to a filterable virus, but American workers have been unable to identify the causative agent. An acute onset with high fever precedes a toxic stage lasting some 7 days. Shock is a common feature in the early part of the toxic

stage and is followed by renal failure with a haemorrhagic diathesis. Postmortem examination of the lungs reveals oedema, congestion, and focal areas of haemorrhage.

Radiological examination in 181 cases at the U.S. Army Hospital, Osaka, revealed abnormality in the chest in 26. In 2 cases there was moderate distension of the small and large bowel, suggesting paralytic ileus. The lung fields showed congestion of the pulmonary vessels and, with increasing congestion, patchy opacities becoming confluent and chiefly central in distribution. In some cases there were peripheral opacities which were probably due not to renal or cardiac failure but to focal areas of vascular congestion. The central opacities were considered to be due primarily to renal failure. Terminally, pulmonary oedema was extreme, leading to complete obliteration of all lung detail.

[The reproductions of radiographs taken in non-fatal cases show oedema shadows with typical " bat's wing " distribution or large areas of peripheral opacity. In each case there is the characteristic rapid progression or regression of the lesions which is seen in pulmonary vascular disturbances—for example, in acute nephritis, periarteritis nodosa, and allergic conditions.]

Kenneth A. Rowley

1510. **Splenic Venography**

N. R. KONAR and A. N. SEN GUPTA. *British Medical Journal* [*Brit. med. J.*] **2**, 810–812, Oct. 10, 1953. 5 figs., 9 refs.

The authors report their experience with the technique of splenic venography described by Dreyer and Budtz-Olsen (*Lancet*, 1952, **1**, 530; *Abstracts of World Medicine*, 1952, **12**, 293). Briefly the method consists in injecting the opaque medium into the spleen itself as quickly as possible (within 5 seconds), the exposure being made immediately the full amount of the dye has been injected. Using a dose of 20 ml. of iodoxyl the present authors found that great force was required for the injection if a fine lumbar-puncture needle was used. They therefore substituted a larger, adult-type needle, which permitted a faster injection and caused no complications. If the spleen was found to be enlarged, the needle was pushed about 5 cm. into the splenic tissue, but in most cases a distance of 3 to 4 cm. was enough.

The procedure was carried out at Nilratan Sarkar Medical College, Calcutta, on 2 control subjects, 2 patients with portal hypertension, 3 with cirrhosis of the liver, and 7 with splenomegaly of unknown origin. In some cases the patient complained of pain over the splenic area which lasted for about 10 minutes. No alteration in pulse, respiration rate, or temperature was noted, and the patient was allowed up and showed no ill effects in all except one case, in which there was a mild fever for a few days.

In the normal splenic venogram the splenic vein, the portal vein, and the branches of the latter inside the liver are visible, and a small portion of the superior mesenteric vein near its entry into the splenic vein can be made out. In cases of obstruction of the splenic vein the portion beyond the constriction is not shown. In portal hypertension the blood flow may be reversed owing to the greatly increased pressure in the portal circulation, and the medium may enter the inferior mesenteric and left gastric veins. In cirrhosis of the liver the intrahepatic branches of the portal vein may be visible, but are only very faintly seen. The degree of prominence and the tortuosity of the mesenteric and gastric veins provide a measure of the degree of portal hypertension present.

The authors did not find any evidence of portal hypertension in their cases of splenic enlargement of unknown origin; the splenic and portal veins were dilated and tortuous and were fainter in outline than in normal cases. In these patients, as well as in some cases of cirrhosis of the liver, these vessels were sometimes so dilated as to resemble loops of intestine. *J. Rabinowitch*

1511. **The Detection of Liver Metastases by Transparietal Splenoportography.** (La détection des métastases hépatiques par spléno-portographie transpariétale) L. LEGER, C. PROUX, and J. ARNAVIELHE. *Presse médicale* [*Presse méd.*] **61**, 1522–1523, Nov. 18, 1953. 2 figs., 7 refs.

The authors point out that even at laparotomy it is not always possible for the surgeon to exclude the presence of malignant metastases in the liver, as only those which are superficial and in a position to be palpated can be recognized. Proper palpation is impossible where the primary tumour is outside the abdominal cavity.

In this paper 2 cases are described in which a preoperative diagnosis of liver metastases was made by splenoportography, 20 ml. of 70% diodone being used as the opaque medium. The first patient, a woman of 55, had had her breast removed for carcinoma; 6 months later she returned with an enlarged and painful liver accompanied by pyrexia, the symptoms being suggestive of liver abscess. Splenoportography showed absence of filling of the portal vein and its intrahepatic branches and there was a dilated collateral vessel. Subsequent laparotomy confirmed the presence of metastases in the liver. The second case, one of carcinoma of the rectum in a woman aged 70, showed no clinical evidence of metastases, but repeated splenoportography revealed a notching of the intrahepatic branches of the portal vein in a position which was subsequently shown to correspond to a metastasis. At operation multiple metastases of the liver were found.

John H. L. Conway-Hughes

1512. **Salpix. A New Approach to the Ideal Radiopaque Medium for Hysterosalpingography**

I. C. RUBIN, E. MYLLER, and C. G. HARTMAN. *Fertility and Sterility* [*Fertil. and Steril.*] **4**, 357–370, Sept.–Oct., 1953. 6 figs., 46 refs.

The authors describe a new preparation which they have used with success for hysterosalpingography at the Mount Sinai Hospital, New York. They suggest that a radio-opaque medium, to be satisfactory for this purpose, should fulfil the following criteria: (1) it should be dense enough to cast a clean shadow; (2) it should pass through the Fallopian tubes slowly enough to allow radiographs to be taken; (3) it should be sufficiently viscous to enable

strictures of the tubal lumen to be accurately visualized; and (4) all material injected should be completely resorbed within a few hours, leaving no trace behind in the tubes or in the peritoneal cavity.

The new substance, "salpix", is a combination of a solution of polyvinylpyrrolidone (P.V.P.) with sodium acetrizoate (3-acetylamino-2:4:6-triiodobenzoate) which has an iodine content of 65·8%. Salpix is stable on storage for 6 months at 50° C. and may be autoclaved without loss of its desirable properties. This medium has now been employed by the authors in over 350 cases and has all the advantages of the iodized oils as well as being water-soluble, enabling tubal obstruction to be diagnosed from a single radiograph and obviating the need for patients to return 24 hours later for further examination. No pelvic irritation occurred in any of the cases examined. Salpix is absorbed within 1 or 2 hours, and no trapping occurs at constricted points in the tubal lumen. It therefore did not give rise to a foreign body granuloma or total obstruction in any of the authors' cases.

The authors consider salpix to be the ideal contrast medium for use in hysterosalpingography.

J. Rabinowitch

1513. **Arthrography of the Knee.** (L'arthrographie du genou)

J. ARCHIMBAUD. *Journal de radiologie, d'électrologie et Archives d'électricité médicale* [*J. Radiol. Électrol.*] **34**, 623–633, 1953. 22 figs., 4 refs.

After trying various methods of arthrography of the knee-joint employing air, contrast media, and double contrast, the author has come to the conclusion that simple arthrography, with air only, gives all the necessary information. In the method used at the Hôpital Saint-Luc, Lyons, 2 or 3 ml. of a 1% solution of procaine is injected in the depression behind the outer border of the patella almost as deep as the capsule. Through a small intravenous needle, inserted until it almost touches the articular surface of the patella, any effusion which may be present is completely aspirated. Some 80 to 100 ml. of air is then introduced, slight flexing movements being made to help dispersion while this is being done, and the suprapatellar pouch being palpated to make certain that the air is actually entering the joint space. Contrary to the practice of most workers, no Esmarch bandage is placed over the suprapatellar pouch. The patient is then turned on his face, and asked to flex and extend the joint several times. It is important for the centre of the *x*-ray beam to pass through the line of articulation; this is situated 4 cm. below the popliteal fold and this point should be marked with a skin pencil. The knee-joint is now flexed through 10 degrees by allowing the leg to rest on the dorsal surface of the big toe. In order to bring the menisci into view, a valgus displacement must be made to expose the internal meniscus and a varus displacement for the external; three tangential views are taken for each meniscus. The intercondylar notch is examined by flexing the knee through 80 degrees and using a ray tangential to the upper end of the tibia. When arthrography is finished the air is aspirated as completely as possible; any remaining air is absorbed within a few days, during which time the patient is advised to rest.

A persistent synovitis seldom results from arthrography, and indeed some hydrarthroses disappear rapidly after the examination. No case of purulent arthritis was encountered in the author's series of 400 cases.

The normal and pathological appearances to be expected in the joint are discussed in detail. The 400 cases are divided into two series: in the first (125 cases), 52 were operated on and there were 6 radiological diagnostic errors; in the second (275 cases), 68 were operated on and there were 2 radiological errors. In 3 cases joints which were operated on in spite of normal radiological appearances were all found to be normal.

John H. L. Conway-Hughes

1514. **An Analysis of the Radiological Findings in 20 Cases of Osteoblastic Osteogenic Sarcoma**

J. H. E. BERGIN. *British Journal of Radiology* [*Brit. J. Radiol.*] **26**, 628–637, Dec., 1953. 5 figs., 8 refs.

It is first pointed out that the diagnosis of osteogenic sarcoma depends upon clinical, radiological, and pathological evidence, each of which is of fundamental importance, and that mistakes may occur if the diagnosis is based on only one of these.

As regards radiological examination, the author emphasizes the need for multiple films taken with varying degrees of rotation of the limb, and for films taken with different penetration to show the soft tissues in addition to bone detail. Serial films should be obtained with the same technique after an interval of some weeks or months. He analyses 20 cases of osteogenic sarcoma selected from the Bristol Bone Tumour Registry. In 15 of these the clinical, radiological, and pathological findings were typical. Of the 5 patients with atypical symptoms, 3 survived for a long time after treatment, one of them being free from any sign of recurrence for 6 years, when metastases developed in the lung.

The author suggests that the prognosis is best in cases which are typical histologically, but atypical clinically and radiologically. The tumour in these cases is probably of low malignancy, and a relatively long survival time is to be expected, whatever the treatment. In prognosis in these cases serial radiographs are of more help than histology.

D. E. Fletcher

1515. **Radiological Studies of Bone Structure in Albers–Schönberg Disease.** (Röntgenologische Studie zur Knochenstruktur bei der Albers–Schönbergschen Erkrankung)

G. LIESS and E. DÖRFFEL. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **79**, 713–727, Dec., 1953. 11 figs., bibliography.

1516. **Evaluation of Routine Serial Fluoroscopic Examinations of the Heart in the Postero-anterior and Oblique Views at Specific Degrees of Rotation. With Special Reference to the Angle of Clearance of the Left Ventricle**

M. G. WILSON, N. EPSTEIN, H. N. HELPER, and K. HAIN. *Circulation* [*Circulation (N.Y.)*] **8**, 879–882, Dec., 1953. 1 fig., 6 refs.

History of Medicine

1517. **The *De Officio Magistratus* of Johannes Ewichius. A Sixteenth Century Treatise on Preventive Medicine**
J. RITCHIE. *Edinburgh Medical Journal* [*Edinb. med. J.*] **60**, 437–451, Nov., 1953. 10 refs.

Johannes Ewichius (1525–88) was born at Cleves in the Netherlands, studied philosophy at Cologne and Paris and then medicine at Padua and Venice, and was for twenty-six years Town Physician of the Free City of Bremen, a post equivalent to that of the Medical Officer of Health of today. One of the chief problems confronting such an officer at that time was the prevention and control of epidemics of plague, and in his book, entitled for short *De Officio Magistratus*, Ewichius sets out the principles by which he and the municipal authorities should be guided. First published in Latin in 1582, it was translated into English by John Stockwood (1583) and into German by Möller (1584), a second Latin edition appearing as late as 1656.

The full Latin title of the work might be translated as "On the Duty of a faithful and prudent Magistrate in preserving and delivering the Commonwealth from Infection in time of Pestilence". It shows Ewichius as a thoughtful, observant, practical, and humane physician. Few of his ideas were novel, although many of them must have still seemed Utopian to his contemporaries. The first part of the work deals with the protection of the general public, and the second with the care of the plague-stricken. He stresses the responsibility of the magistrates for controlling epidemics, and lays down rules for sanitation, quarantine, the establishment of a corps of plague doctors and of special plague hospitals, and for the housing and feeding of those who have taken to the roads to escape from plague centres. Like most of his contemporaries he sought the pathological cause of plague in effluvia and fomites and so insisted on the prophylactic value of fresh air, sunlight, and scrupulous public and personal cleanliness.

Much of what Ewichius had to say of hygiene in the 16th century was still applicable, and was repeated in much the same form, during the severe cholera epidemics of the 19th century. *F. N. L. Poynter*

1518. **Jan Evangelista Purkyně. Czech Scientist and Patriot (1787–1869)**
H. J. JOHN. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **46**, 933–940, Nov., 1953. 2 figs., 18 refs.

Surprisingly little has been published in English about the life and character of Purkyně; this the author attributes, in part at least, to the fact that in many of his accomplishments he was ahead of his time and therefore not properly appreciated by his contemporaries. The author refers to his early association as student and teacher with the Piarist Order, and to his considerable linguistic ability (he spoke 13 languages). After three years as assistant in anatomy and physiology at the University of Prague, Purkyně was appointed to the Chair of Physiology at the University of Breslau. He occupied the chair for 27 years, during which time he established the first physiological institute in Europe and accomplished his most important scientific work. In 1850, at the age of 63, he returned to Prague as Professor of Physiology, where he established a second institute of physiology.

Purkyně's earlier life was spent in an atmosphere of frustration and prejudice created by the political situation of his time; in spite of this, the lack of adequate space and facilities for research, and his family troubles, he worked unceasingly on a great variety of problems. His methods of teaching met with disapproval, for he was not content to repeat the theories of the old masters but insisted on practical demonstrations and on performing experiments in animals. For this purpose he established his first laboratory in an unoccupied corner of the college building which had been assigned to him at the University of Breslau, but he met with so much opposition that he transferred it to his own home, where he lived, dined, and slept in rooms crowded with instruments and equipment and animals for experimental work. His output, when viewed against this background, is amazing. It took him nine years to get his first microscope, but as his work became known the respect of his colleagues increased; in 1839 the Prussian Government erected for him a separate building to be devoted exclusively to physiology.

Purkyně's first researches were in the physiology of vision; indeed optical phenomena remained one of his chief interests, as shown by the figures, images, and phenomenon named after him. Many of his discoveries were forgotten or were not utilized until a much later date. He discovered, for example, the principle of illumination of the ophthalmoscope and recommended its use in the diagnosis of eye affections, but it was 24 years before this recommendation was adopted.

His name is best known, however, in connexion with cellular anatomy. He was the first to realize the significance of the cell as the unit of life and to emphasize the analogous microscopic structure of plant and animal; he introduced the word "protoplasm" to scientific literature. In 1837 he reported his discovery of the ganglion cells in the grey matter of the brain. In every branch of physiology he made discoveries of the utmost importance—in histology and in the functional physiology of the heart and digestive and respiratory systems; in each he devised and perfected the necessary instruments for recording his results. He was also the first to advocate a system of classification of finger prints.

At the same time Purkyně was a pioneer in the establishment of modern methods in medical education and took an active part in numerous cultural societies, translating the works of Schiller, Goethe, and other Ger-

man writers into Czech. After his return to Prague in 1850 he devoted himself increasingly to politics (he was a member of the Senate) and to literary work. The range of his interests seemed limitless, and in all that he did he " displayed clarity of thought, thoroughness, purpose, and perseverance ". He died in 1869, mourned by people of every class in Bohemia. *D. P. McDonald*

1519. **Leonard Gillespie (1758–1842). Naval Surgeon and Physician to Lord Nelson**
J. J. KEEVIL. *Journal of the Royal Naval Medical Service* [*J. roy. nav. med. Serv.*] **39**, 229–240, 1953.

The author gives some account of the life of a naval surgeon whose chief claim to distinction was the fact that in November, 1804, he was appointed physician to the Mediterranean Fleet and took up his duties in the *Victory*. On January 20, 1805, when, before the action at the Maddalena Islands, Nelson gave the general signal " Prepare for Battle ", Gillespie wrote to his sister: " For my own part I behold with great coolness the enthusiasm of all around me in anticipating the laurels to be gained in the expected battle. I regard such things as necessary evils in which every man is bound to do his duty to the utmost of his power and not as a matter for any great degree of exultation ". As the author points out, it was significant " that he should have used almost the very words of the famous signal which was to be made on October 21, under identical circumstances ". Gillespie was not, in fact, present at Trafalgar, as he had resigned his appointment on account of ill-health in August, 1805.

Gillespie is presented as a man of ideas and not as a pioneer or discoverer. An acute observer of the contemporary scene, he kept diaries in which he recorded his opinion on such issues as slavery, crime and punishment, war, international relations, and much else. The author states: " I do not claim for him that he was responsible for a more humane and thoughtful attitude in the Navy, but I believe that through his influence and through that of men like him, a movement was accelerated and took clearer form, a movement which was eventually expressed in Admiralty orders, but was not the outcome of them, a movement which was started by the constant pressure of ordinary men most of whom are now forgotten. Similarly I do not claim for Gillespie that he suggested the words of the famous signal at Trafalgar, but I think that something that he said did influence its form ".
D. P. McDonald

1520. **Frederik Holst's Description of the " Tetralogy of Fallot " in 1832.** (Frederik Holsts beskrivelse av " Fallot's Tetrade " i 1832)
S. AARSETH. *Tidsskrift for den Norske Lægeforening* [*T. norske Lægeforen.*] **73**, 799–801, Nov. 1, 1953. 2 figs., 7 refs.

Frederik Holst (1791–1871) was Professor of Hygiene and Pharmacology in the University of Oslo and editor of Norway's first medical journal, *Eyr*. In 1832 he published in that journal a description of a case of congenital heart disease which was almost identical with the condition described 56 years later by Fallot, and thereafter known as the tetralogy of Fallot. The patient, a girl, had come under Holst's care in 1823 at the age of 5 and he attended her until her death 2 years later. In his paper he described the cyanosis, clubbing of the fingers, dyspnoea on the slightest exertion, the loud precordial murmur (heard with a Laënnec stethoscope), the crouching position assumed by the patient, the subnormal temperature, the haemorrhagic tendency, and the dark, thick blood. Post-mortem examination revealed three of Fallot's classic signs—a large right ventricle, a ventricular septal defect, and a small overriding aorta—and a small (though not apparently stenosed) pulmonary artery. It is of interest to note that Holst was using Laënnec's stethoscope in Norway in 1823, only five years after the publication in Paris in 1818 of Laënnec's paper on auscultation. *B. Nordin*

1521. **Pierre Marie 1853–1940**
H. COHEN. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **46**, 1047–1054, Dec., 1953. 1 fig., 16 refs.

It is a curious fact that when Pierre Marie died in 1940 no obituary notice appeared in any of the medical journals of Britain. The present author, in a paper read before the Royal Society of Medicine in the centenary year (1953) of Marie's birth, remedies that omission with a full-length portrait of the man and his work, based upon personal knowledge. As the author states: " Fifty years of productive clinicopathological researches and the bringing to bear of so powerful an analytical mind, encouraged by his early training, on the philosophical questions which these posed, cannot be compressed into a brief address ". Nevertheless, the portrait is a living one.

Marie was called to the French bar before he studied medicine, and his maturity brought with it a knowledge of several languages and of ancient history, and a deep appreciation of art which may well have explained his brilliantly acute powers of observation. At 25 he was admitted to a hospital internship under the two most distinguished professors of the Faculty of Medicine in Paris—Bouchard, the pathologist, and Charcot, the eminent neurologist, to whom he was in turn clinical chief, laboratory chief, and private assistant. Marie qualified in 1883. In 1888 he was appointed physician and in 1889 *professeur agrégé* in the Faculty of Medicine; during this period he delivered his lectures on " Diseases of the Spinal Cord ", which were subsequently published. It was in the years between 1897 and 1907, when Marie was at the Hospice de Bicêtre, that his main contributions to neurology were made. In 1907 he succeeded Cornil in the Chair of Pathological Anatomy in the Faculty of Medicine, and it was not until 1917, when he was appointed to the Chair of Clinical Neurology at the Salpêtrière—the hospital in which he had worked with Charcot forty years before—that his old interest in neurological research returned; the war years, however, were not favourable for major research.

Within three years of qualification, Pierre Marie described, with Charcot, the distinguishing symptoms of peroneal muscular atrophy. His first independent major

contribution was made the same year, when he described 2 cases of acromegaly, and differentiated the condition from Paget's disease, myxoedema, and leontiasis ossea. Acromegaly had Marie's continuing interest, and modern knowledge of the pituitary stems largely from his work. In 1890 he had differentiated pulmonary osteoarthropathy from acromegaly, and in 1898 his first paper on spondylitis appeared. In 1893 he described the " new anatomoclinical entity " of hereditary cerebellar ataxia. His profound study of the problems of aphasia were carried out between 1901 and 1906. Marie's many important contributions to neuropathology are collected, with his major works, in his *Travaux et mémoires*, first published in 1926.

Outwardly, Marie " was severe, authoritative, preserving the dignity and jealous of the rights of a Chief, but at heart he was warm, sympathetic, affectionate. If he had strict rules for his assistants, it was because he imposed them on himself, and expected from those who worked with him the same industry, zest, and conscientiousness ". *D. P. McDonald*

1522. **Centenary of Hypodermic Injection**
G. A. MOGEY. *British Medical Journal* [*Brit. med. J.*] 2, 1180–1185, Nov. 28, 1953. 6 figs., 31 refs.

The modern hypodermic syringe and needle have evolved from cruder predecessors made for intravenous injection and blood transfusion. In 1657 Christopher Wren conducted a number of experiments, with the assistance of Robert Boyle and a Dr. Wilkins, on the intravenous injection of blood and drugs into man and animals. In this early work a quill, which was later replaced by a silver or gold tube, was inserted into the vein and the injection made through it by means of a small bladder acting as a pump or by gravity feed. Because drugs were impure and the apparatus was crude intravenous medication fell into disuse, but interest in it was revived at the end of the 18th and the beginning of the 19th centuries by Majendie and others. Pravez, in 1853, designed a syringe for the injection of perchloride of iron into aneurysms with a view to coagulating the contained blood. In 1844 Rynd, a Dublin surgeon, injected solutions of opium into patients suffering from sciatica and neuralgia and has therefore been held by some to have initiated the technique of hypodermic injection, but although he used a hollow cannula, which may be regarded as a forerunner of the hypodermic needle, he relied upon gravity and not upon a syringe to force the solution into the tissues. Further, he was interested only in the local pain-relieving properties of the injection.

In 1853 Dr. Alexander Wood, of Edinburgh, made the first injection through the skin by means of a syringe and needle. During injection of a naevus with perchloride of iron by the Pravez method, he conceived the idea of using the syringe and needle for injecting a solution of morphine close to the nerve in cases of neuralgia. Although Wood, like Rynd, was chiefly interested in relieving pain by local injections, he realized the potentialities of this new technique. In the conclusion to his article on the subject (*Edinb. med. surg. J.*, 1855, **82**, 265) he stated that " the effects of narcotics so applied are not confined to their local action, but . . . reach the brain through the venous circulation and there produce their remote effects . . . In all probability what is true in regard to narcotics would be found to be equally true in regard to other classes of remedies ". Some credit for the introduction of " hypodermic " injection of narcotics for their remote effects must be given to Charles Hunter, a London surgeon, who used drugs other than morphine and developed the " grandiose idea of the hypodermic treatment of disease ". Wood had previously used the term " subcutaneous injection " to describe the method.

The syringe used by Wood is in the Museum of the Royal College of Surgeons of Edinburgh.

Ruth Hodgkinson

1523. **The Cause of Beethoven's Deafness.** (Woran litt Beethoven?)
H. BEYER. *Ärztliche Wochenschrift* [*Ärztl. Wschr.*] **8**, 1105–1107, Nov. 13, 1953. 6 refs.

As scientific otology was unknown in Beethoven's time, the cause of his deafness can only be deduced from information gleaned from his letters and the records of his conversations. It is possible that the chronic colitis from which Beethoven suffered (and which was for long erroneously regarded as typhoid in nature) may have affected his hearing, but although he himself apparently subscribed to this theory, he also stated that the onset of deafness preceded that of the colitis. Subsequently he developed acute otitis media during an attack of fever, and after this he appears to have heard tones incorrectly, at times accusing the violins of playing in the wrong key. This may have been due to a serous otitis, the formation of adhesions in the middle ear producing the troublesome whistling from which it is known that Beethoven suffered severely. A further deterioration followed a severe fall on the back, after which his deafness became almost complete and his hearing never improved. It seems probable, however, that the primary condition was one of severe and progressive otosclerosis, both auditory nerves being found at necropsy to be reduced in size, the left nerve being much thinner than the right. This diagnosis is supported by the characteristic observations made by Beethoven on his deafness—he heard voices well, but could not understand the words, and found it highly unpleasant when anyone spoke too loudly to him.

With his increasing deafness Beethoven devoted himself less to music, and spent more time in the company of friends, where he could hope that his difficulty in hearing might sometimes pass unnoticed and his failure to respond to a question be attributed to absentmindedness. To understand his attitude towards his deafness —" the demons in his ears ", as he called it—its effect on his social activities must be appreciated. With his striking appearance and his deep, sonorous voice, he was lionized in the salons and sought after by the aristocracy, and although he tried to conceal his deafness, the increasing difficulty of human intercourse made him feel cut off from all that he valued most in life. Malzel, the

inventor of the metronome, made him an ear trumpet, but Beethoven used it little, probably because it drew attention to his disability. In conversation he preferred the safety of the written word to the misunderstandings which arose from imperfect hearing, and his " conversation books " were the result.

His last public performance on the piano was in 1815, when he accompanied the singer Wild, and he must have given up regular conducting before this. Nevertheless he insisted on conducting *Fidelio* in 1821, with disastrous results, and although he had greater success later in conducting the first performances of his Ninth Symphony and the Missa Solemnis, his deafness was such that he was quite unaware of the frenzied applause of the audience until one of the singers turned him to face them. The intensity of his inner musical life and the perfection of his inner spiritual ear were almost unbelievable. " Where my ideas come from I cannot say," he wrote, " they come uncalled, communicable and incommunicable. I can grasp them with the hand in the open air, walking in the woods, in the quiet of the night, in the early morning, excited by emotions which the poet translates into words and I into music, until finally the notes stand before me." *J. G. Bonnin*

1524. **The Life of the Shawl**

D. HUBBLE. *Lancet* [*Lancet*] **2**, 1351–1354, Dec. 26, 1953. 12 refs.

In the 16th and 17th centuries the seat of hypochondria was considered to be the liver, the gall-bladder, and the spleen; in the 18th century hypochondria was a fashionable malady; only in the 19th century was it accurately described as being " characterised by the patient's unfounded belief that he is suffering from some serious bodily disease ". Today it is also associated with some " over-care " in the patient's environment, concern with precautions against ill-health, and immaturity in the personality of the patient. Evidence that Charles Darwin's ill health was hypochondriacal is to be found in his autobiography, in his children's reminiscences, and in family letters, though neither in him nor in his sons, of whom 4 became eminent scientists, did hypochondria detract from intellectual achievement. The wearing of a shawl was a sign of ill health with the Darwins, and in the present paper the author gives some account of the history of illness and hyponchondria in the families of Robert Darwin and his son, Charles, both of whom married into the Wedgwood family. (The author acknowledges his debt to Mrs. Raverat's book, *Period Piece*, which provides much new evidence from the Darwin family records.)

Robert Darwin was so successful as a practitioner in Shrewsbury that he amassed sufficient money to ensure the security of his children and grandchildren. He was, however, a tyrannical father. His 4 daughters were disagreeable and bad-tempered both as children and in later life, and his son, Erasmus, though he lived to the age of 72, was described by Carlyle as being " doomed to silence and patient inertia ". Robert Darwin's wife, Susannah Wedgwood, died when Charles was only 8½ years old.

Charles's attitude towards his father, as towards opponents in later life, was one of gentleness and tolerance, even of affection; his aggression always turned inwards—to guilt, insomnia, and digestive troubles. His first hypochondriacal illness occurred before his marriage, in 1831, when he suffered great depression while waiting for the *Beagle* to sail. In 1839 he married Emma Wedgwood; he became ill during her first pregnancy the following year and was incapable of sustained work throughout the succeeding two years. They moved to Downe in Kent in 1842, and Emma was always thereafter the nurse, providing perhaps the over-care absent from his home.

Charles and Emma Darwin had 10 children, and for the 7 who lived to adult life Down House provided an ideal environment of security and love. Emma was a loving mother and a perfect nurse, while Charles was full of anxious sympathy, especially after the death of his daughter Annie. But of these 7 children, 5 suffered from hypochondria. Henrietta was an " invalid " from the age of 12 until her death at the age of 86, and loved illness in others; George suffered from ill health; Leonard resigned from the army at the age of 40, though he lived to be 93; Sir Francis suffered from depression; Sir Horace, the youngest, was both frail and retarded; only Elizabeth and William escaped.

The true conclusion to be drawn from a study of these family histories is the importance of environment in the development of personality. " The Darwin–Wedgwood union in Shrewsbury at the turn of the century had resulted in disagreeable and unfulfilled daughters, and neurotic sons; the same prescription a generation later in Downe was to produce a large family growing in unexceptionable happiness to remarkable fulfilment—children of delightful personality but dangerously disposed to invalidism ". *W. J. Bishop*

1525. **St. Thomas's and the Private Schools of Anatomy**

F. A. TUBBS. *St. Thomas's Hospital Gazette* [*St Thom. Hosp. Gaz.*] **51**, 244–246, Dec., 1953. 1 fig., 4 refs.

Private lectures in anatomy and surgery began about the same time and for the same reason as the lectures at the " oldest anatomical school in London ", St. Thomas's. William Cheselden, surgeon at St. Thomas's, was the first successfully to break the " exclusive rights " of the Barber Surgeons to teach surgery and anatomy; in 1711, at the age of 22, he gave his first private lectures. His example was followed by Edward Nourse, surgeon at St. Bartholomew's, who began to lecture on anatomy about 1730 at his house in Aldersgate Street. Percivall Pott, who was Nourse's assistant, started giving private lectures in 1747; the notebooks of two of Pott's students are in the possession of the Medical School Library at St. Thomas's. Other leading men among the lecturers at these private schools were William and John Hunter, George Fordyce, Joshua Brookes, and Edward and Richard Grainger. Some of these private schools gave long and valuable service, others were mushroom growths, lasting a few months only; they disappeared from the medical scene about 1850, by which time they had outlived their purpose. *Calvin P. B. Wells*